Collodion baby case series: the success of oral retinoic acid

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Abstract
Ichthyosis is a clinical skin cornification disorder characterized by hyperkeratosis. Lamellar ichthyosis is a rare form of ichthyosis (collodion baby), which is autosomal recessive. Diagnostic clinical findings can be confirmed with skin biopsy and genetic analysis. The principles of treatment are moisturizing the skin, prevention of dehydration, and use of keratolytic agents. Systemic retinoic acid (0.5-1 mg/kg/day) is reported to provide dramatic benefits in the treatment of lamellar ichthyosis and congenital ichthyosiform erythroderma. In this study, the efficiency of oral retinoic acid treatment is presented to show a dramatic improvement in five patients who were diagnosed as collodion babies and admitted to The Neonatal Intensive Care Unit after birth. None had other congenital problems. Only two patients were diagnosed as having sepsis. Hair loss was the only adverse effect of treatment in all five patients. With this series of collodion baby, we wanted to draw the attention of physicians to the promising efficacy of retinoic acid.

Keywords: Collodion baby, newborn, retinoic acid

Introduction
Collodion baby (congenital lamellar ichthyosis) is a cornification disorder that is clinically characterized by exfoliation in the skin and histopathologically characterized by hyperkeratosis. Affected babies are born with a collodion membrane. In this disease, which is characterized by large squamous, parchment-like eruptions on the skin, extrverted palpebrae and overturned lips are determinative findings; erythrodermia and mucosal involvement are not observed. The diagnosis is made with clinical findings, skin biopsy, and genetic tests. The principles of treatment include humidification of the skin, prevention of fluid loss, and use of keratolytic agents. Eye care is also required for extrverted palpebrae. It has been reported that systemic retinoic acid (0.5-1 mg/kg/day) treatment provides a dramatic benefit in severe forms of ichthyosis including colloidon baby and congenital ichthyosiform erythroderma (1, 2).

Long-term use of systemic retinoid has been reported to cause teratogenic and toxic effects in bone tissue, effects on bone mineralization and osteophytes, and calcification in ligaments. Cheilitis, dryness of mucous membranes, mild hair loss, and pruritus are the other adverse effects of oral retinoids (3, 4). Here, we present five patients who were diagnosed as being colloidon babies after birth who showed dramatic improvement in clinical findings after treatment with retinoic acid.

Case 1
Our first patient was born at term by spontaneous vaginal delivery from the first pregnancy of a 19-year-old healthy mother and a 20-year old father who had second-degree consanguinity. The Apgar scores in the first and fifth minutes were assessed as 10/10. On physical examination, the body weight was 2400 g, the height was 47 cm, and the head circumference was 33 cm,
which was within the normal percentile range. Diffuse parchment-like lamellar exfoliation and yellow, scaly eruptions were found on the whole body including the scalp, face, palms, and soles. The palpebrae were extra-vverted and the lips were overturned. Other system examinations were found as normal. A diagnosis of colloidon baby was made with clinical assessment (Picture 1). The patient was hospitalized in the neonatal intensive care unit (NICU). Care was given in a humidified incubator. Daily bathing and oil bath with liquid vaseline was initiated. Intravenous fluid treatment and empiric antibiotic treatment was initiated. On the third day of hospitalization, retinoic acid treatment at a dosage of 1 mg/kg/day was initiated. Echocardiography, abdominal ultrasonography, and cranial ultrasonography were performed and found to be within the normal limits. Thyroid functions were found to be normal. On the fifth day, C-reactive protein was found to be positive. Teicoplanin treatment was initiated after samples were obtained for sepsis screening. On the 10th day, extraverted palpebrae, the overturned lips and skin findings showed marked improvement (Picture 2). On the 20th day, retinoic acid treatment was switched to alternate day treatment. Meropenem was added to treatment on the 28th day when CRP was found to be increased. Erythrocyte suspension was transfused because of anemia. Flucanazole was added to treatment on the 31st day because *Candida albicans* grew in a blood culture. A thrombocyte suspension was transfused because of thrombocytopenia. In the follow-up, no disruption in liver function tests was observed. On the 40th day, the patient was discharged to use retinoic acid two days a week. In the outpatient follow-up, liver functions tests were found to be normal. Retinoic acid was discontinued at the age of two months. Hair loss due to the use of retinoic acid was observed. No complications were observed at the follow-up visit performed at the age of five months.

**Case 2**

Our second patient was born at term by spontaneous vaginal delivery from the fifth pregnancy of a 38-year-old healthy mother and a 42-year-old father who had second-degree consanguinity. The Apgar scores in the first and fifth minutes were assessed as 9/10. On physical examination, the body weight was 3200 g, the height was found to be 52 cm and the head circumference was 36 cm, which was within the normal percentile range. Diffuse parchment-like lamellar exfoliation and yellow, scaly eruptions were found on the whole body including the scalp, face, palms, and soles. The palpebrae were extraverted and the lips were overturned (Picture 3). Other system examinations were found to be normal. In the family history, it was learned that a male sibling was born with similar findings and died in the neonatal period. A diagnosis of colloidon baby was made with clinical assessment. The patient was hospitalized in the NICU. Care was given in a humidified incubator. Daily bathing and oil bath with liquid vaseline was initiated. Intravenous fluid treatment, empiric antibiotic treatment, and retinoic acid treatment at a dosage of 1 mg/kg/day was initiated. Echocardiography, abdominal ultrasonography and cranial ultrasonography were performed and found to be within the normal limits. Thyroid functions were normal. On the 8th day, the extraverted palpebrae, overturned lips, and skin findings showed marked improvement (Picture 4). On the 12th day, retinoic acid treatment was switched to alternate day treatment. The patient was discharged to use retinoic acid two days a week. On the 45th day, he was hospitalized with a diagnosis of severe anemia and erythrocyte suspension was transfused. The causes of
anemia were investigated; a bone marrow aspiration was performed and assessed to be normocellular. In the follow-up, no disruption in liver function tests was observed. In the outpatient follow-up, liver function tests had a normal course. Retinoic acid was discontinued at the age of two months. Hair loss due to the use of retinoic acid was observed. No complications were observed in the follow-up visit performed at the age of four months.

Case 3

Our third patient was born at term by spontaneous vaginal delivery from the fifth pregnancy of a 28-year-old healthy mother and a 32-year-old father who had no consanguinity. The Apgar scores in the first and fifth minutes were assessed as 8/10. On physical examination, the body weight was 3100 g, the height was 50 cm, and the head circumference was 34 cm, which was within the normal percentile range. Diffuse parchment-like lamellar exfoliation and yellow, scaly eruptions were found on the whole body including the scalp, face, palms, and soles. The palpebrae were extrverted and the lips were overturned (Picture 5). Other system examinations were found as normal. A diagnosis of colloidon baby was made with clinical assessment. The patient was hospitalized in the NICU. Care was given in a humidified incubator. Daily bathing and oil bath with liquid vaseline was initiated. Intravenous fluid treatment, empiric antibiotic treatment, and retinoic acid treatment at a dosage of 1 mg/kg/day was initiated. Echocardiography, abdominal ultrasonography and cranial ultrasonography were performed and found within normal limits. Thyroid functions were found as normal. On the 7th day, the extraverted palpebrae, overturned lips, and skin findings showed marked improvement (Picture 6). On the 11th day, the patient was discharged to use retinoic acid two days a week. Liver function tests were found to be normal. In the outpatient follow-up, liver function tests had a normal course. Retinoic acid was discontinued at the age of two months. Hair loss due to the use of retinoic acid was observed. No complications were observed in the follow-up visit performed at the age of three months.

Case 4

Our fourth patient was born at term by spontaneous vaginal delivery from the fifth pregnancy of a 25-year-old healthy mother and a 30-year old father who had...
no consanguinity. The Apgar scores in the first and fifth minutes were assessed as 8/10. On physical examination, the body weight was found as 2950 g, the height was 51.5 cm, and the head circumference was 35.5 cm, which was within the normal percentile range. Diffuse parchment-like lamellar exfoliation and yellow, scaly eruptions were found on the whole body including the scalp, face, palms, and soles. The palpebrae were everted and the lips were overturned (Picture 7). Other system examinations were found to be normal. A diagnosis of collodion baby was made with clinical assessment. The patient was hospitalized in the NICU. Care was given in a humidified incubator. Daily bathing and oil bath with liquid vaseline was initiated. Intravenous fluid treatment and empiric antibiotic treatment was initiated. On the third day of hospitalization, retinoic acid treatment was initiated at a dosage of 1 mg/kg/day. Echocardiography, abdominal ultrasonography, and cranial ultrasonography were performed and found within the normal limits. Thyroid functions were found as normal. On the third day, CRP was found to be positive and vancomycin, amikacin and flucanazole treatment was initiated after obtaining samples for screening sepsis. On the 8th day, it was learned that *Klebsiella pneumonia* was grown in blood culture and meropenem was added to the treatment. On the 12th day, the extraverted palpebrae, overturned lips, and skin findings showed marked improvement (Picture 8). On the 14th day, it was learned that *Staphylococcus epidermidis* was grown in blood culture. An erythrocyte suspension was transfused because of anemia. On the 25th day, retinoic acid treatment was switched to alternate day treatment. On the 30th day, an erythrocyte suspension was transfused because of anemia. No disruption was observed in liver function tests in the follow-up. On the 42nd day, the patient was discharged to use retinoic acid two days a week. In the outpatient follow-up, liver function tests had a normal course. Retinoic acid was discontinued at the age of two months. Hair loss due to the use of retinoic acid was observed. No complications were observed in the follow-up visit performed at the age of two months.

**Case 5**

Our fifth patient was born at term by spontaneous vaginal delivery from the fifth pregnancy of a 30-year-old healthy mother and a 32-year-old father who had no consanguinity. The Apgar scores in the first and fifth minutes were assessed as 8/10. On physical examination, the body weight was 2700 g, the height was 48.2
cm, and the head circumference was 34.3 cm, which was within the normal percentile range. Diffuse parchment-like lamellar exfoliation and yellow, scaly eruptions were found on the whole body including the scalp, face, palms, and soles. The palpebrae were extraverted and the lips were overturned (Picture 9). Other system examinations were found to be normal. A diagnosis of colloidon baby was made with clinical assessment. The patient was hospitalized in the NICU. Care was given in a humidified incubator. Daily bathing and oil bath with liquid vaseline was initiated. Intravenous fluid treatment, empiric antibiotic treatment and retinoic acid treatment at a dosage of 1 mg/kg/day was initiated. Echocardiography, abdominal ultrasonography, and cranial ultrasonography were performed and found within the normal limits. Thyroid functions were found as normal. On the 7th day, the extraverted palpebrae, overturned lips, and skin findings showed marked improvement (Picture 10). On the 11th day, the patient was discharged to use retinoic acid two days a week. Liver function tests were found as normal. In the outpatient follow-up, liver function tests had a normal course. Retinoic acid was discontinued at the age of two months. Hair loss due to use of retinoic acid was observed. No complications were observed in the follow-up visit performed at the age of two months. Written informed consent was obtained from the patient's parents.

**Discussion**

One form of ichthyosis, a cornification disorder characterized by abnormal separation and exfoliation in the epidermis, is lamellar ichthyosis, which is observed considerably rarely (1, 2, 4). In these patients, clinical findings manifest at birth and affected infants are generally born in a colloidon membrane. This membrane separates with exfoliation in 10-14 days and the whole skin is covered with large, grey-brown, thick, parchment-like scales with the edges twisted upwards, adhered in the middle part. Very little or no erythroderma occurs in classic colloidon babies. Findings ranging from a mild increase in streaks to keratoderma may be present on the palms and soles. The lips and mucosa are not involved, but the adjacent skin areas may be. Extraverted palpebrae are observed almost always and diagnostic. Overturning of the lips, reduction in sweating, sweltering, and alopecia may accompany (2). In all our patients, parchment-like lamellar exfoliation was found on the whole body including the palms and soles at birth. Extraverted eyes and overturned lips were prominent. A diagnosis of colloidon baby was made with clinical findings in our patients, none of whom had involvement of oral mucosa and erythrodermia. The specific histopathologic finding is hyperkeratosis in patients with a diagnosis of colloidon baby (4). Heat imbalance and fluid loss occur in these patients because skin integrity is impaired.

Pyoderma and sepsis may be observed in these patients. In addition, complications including pneumonia as a result of aspiration of squamous material in the amniotic fluid in the intrauterine period may be observed and the mortality risk is increased because of all these factors (5). In the literature, it has been reported that renal anomalies, malignant melanoma, polidactilia, thymus atrophy, and thyroid aplasia might be observed in colloidon babies, albeit rarely (6). None of these additional disorders were found in our patients. The principles of treatment include humidification of the skin, prevention of fluid loss, and use of keratolytic agents (2, 4). Lotions, creams, and ointments are used for humidification of the skin, and creams containing 5% lactic or glycolic acid, 10-40% urea and 0.1% retinoic acid are used for keratolytic treatment (2, 4). Eye care for extraverted eyes is also needed in patients with ichthyosis (7). Our patients were monitored in humidified incubators with age and weight-appropriate fluid and electrolyte treatment. It has been reported that systemic retinoic acid treatment (0.5-1 mg/kg/day) provides a dramatic benefit in severe forms of ichthyosis including colloidon baby and congenital ichthyosiform erythroderma (3, 4). It has been reported that long-term use of systemic retinoid may cause teratogenic and harmful effects on the bone tissue; bone mineralization may be affected and osteophytes and calcification in the ligaments may develop (7, 8). Cheilitis, dryness of mucous membranes, mild hair loss, and pruritus are the other adverse effects of oral retinoids (8). In our patients, oral retinoid treatment (1 mg/kg/day in two doses) was initiated in the first three days of life. In the follow-up, extraverted palpebrae, overturned lips, and skin findings showed a marked improvement on the 7-10th day and oral retinoic acid treatment was switched to alternate day treatment (1 mg/kg/day). No adverse effects other than hair loss were observed in our patients. Infection markers were monitored. Antibiotic treatment was adjusted according to the infection markers and culture results. Liver function tests were monitored and were found to have a normal course. The patients were discharged on the postnatal 11-42nd day to oral retinoic acid use two days a week (1 mg/kg/dose). The dose was tapered in the follow-up. No complications were observed in the follow-up of the patients.
Özdemir et al. (9) found a dramatic improvement in eye and skin findings in a colloidon baby they treated with oral retinoic acid and they discharged the patient in the second week of hospitalization. They report no adverse effects related with treatment in the follow-up. Dilek et al. (10) initiated oral retinoic acid treatment in a colloidon baby they followed up, but they decreased the dose and continued treatment when they found disruption in liver function tests.

In conclusion, we aimed to draw physicians’ attention to retinoic acid, which has satisfactory action in the treatment of colloidon baby, by presenting these five patients who showed a dramatic improvement with oral retinoic acid treatment. We think that more experience is needed, however.

References