Collodion Baby Syndrome: A Systematic Review

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ABSTRACT:

Collodion Baby Syndrome is a rare congenital disorder characterized by a tight, shiny membrane covering the neonate’s skin, resulting from various genetic mutations affecting the skin's cornification process. This review comprehensively examines the syndrome's classification, aetiology, pathogenesis, histopathology, clinical manifestations, diagnosis, prognosis, and treatment modalities. Classified under ichthyosis, Collodion Baby Syndrome includes multiple phenotypes, from self-healing collodion baby to harlequin ichthyosis. The pathogenesis involves disruptions in the skin barrier, leading to the formation of the collodion membrane. Histopathologically, there is hyperkeratosis and parakeratosis, with a distinct absence of the granular layer in the epidermis. Clinically, affected neonates exhibit ectropion, eclabium, and digit contractures. Diagnosis primarily involves clinical evaluation, supported by genetic testing to identify underlying mutations. The prognosis varies; while some infants shed the membrane spontaneously, others progress to severe ichthyosis forms requiring lifelong management. Treatment focuses on supportive care to maintain skin integrity and prevent infections. Emollients and keratolytic are cornerstone therapies, while retinoids may be prescribed for severe cases. Recent advances in genetic research and targeted therapies hold promise for improving outcomes. This review emphasizes the need for a multidisciplinary approach in managing Collodion Baby Syndrome, involving dermatologists, geneticists, paediatricians, and ophthalmologists to address the complex clinical needs of affected neonates.

Keywords: Collodion Baby Syndrome, congenital ichthyosis, keratinization, genetic mutations, skin barrier, emollients, retinoids, supportive care, multidisciplinary management.

1. INTRODUCTION:

The word “Collodion Baby” refers to a medical entity for babies that have a translucent, tight, parchment-paper-like skin film covering their entire body surface, known as the collodion membrane. Hallopeau et al coined the term “collodion Baby” in 1884. Approximately 270 instances or cases have been documented since then. Although different diseases (see table no. 1) and circumstances can cause collodion membrane production, the cause is nearly always an autosomal recessive ichthyosiform condition.

Table 1 – List of diseases that can be present in collodion baby

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Name of Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Congenital ichthyosiform erythroderma (particularly the non-bullous variant)</td>
</tr>
<tr>
<td>2.</td>
<td>Lamellar ichthyosis, and harlequin ichthyosis</td>
</tr>
<tr>
<td>3.</td>
<td>Bullous congenital ichthyosiform erythroderma</td>
</tr>
<tr>
<td>4.</td>
<td>Sjogren-Larsson Syndrome</td>
</tr>
<tr>
<td>5.</td>
<td>X-linked to hypohydrotic ectodermal dysplasia</td>
</tr>
<tr>
<td>6.</td>
<td>Gaucher’s disease</td>
</tr>
<tr>
<td>7.</td>
<td>Loricrin Keratoderma</td>
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</tbody>
</table>
Congenital ichthyosiform erythroderma (particularly the non-bullous variant), lamellar ichthyosis, and harlequin ichthyosis (which is commonly thought to be autosomal recessive) are the most common causes. Bullous congenital ichthyosiform erythroderma, Gaucher’s disease, and Sjogren-Larsson Syndrome are all possible associations. [9]

Furthermore, a new autosomal recessive condition known as “self-healing collodion baby” has been identified, in which the newborn recovers completely in a matter of weeks. Because of the relatively severe skin injury, collodion newborns may experience dehydration, electrolyte imbalance, temperature malfunction, and an increased risk of sepsis in the clinic. As a result, the rates of morbidity and mortality in these situations are quite high. To summarize, these neonates should be closely observed in intensive care units and get appropriate and supportive therapy. [21,8]

### Classification of Collodion Baby Syndrome

The technical term for Collodion Baby Syndrome is “ICHTHYOSIS”. This classification of ichthyosis is given by William and Elias in year 1985. They classify ichthyosis into two types, based on molecular, biochemical, histological and genetic criteria. [1,19] These are given below:

1. Non-bullous congenital ichthyosiform erythroderma (NBCIE)
2. Lamellar Ichthyosis (LI)

Other conditions associated with CBS, which is rarely occur, include:

1. Sjogren-Larsson Syndrome
2. Loricrin Keratoderma
3. Annular epidermolytic erythema
4. X-linked to hypohydrotic ectodermal dysplasia

We discuss these types in detail further……

### Lamellar Ichthyosis

Collodion infant can be caused by lamellar ichthyosis. In some circumstances, the skin becomes almost completely erythematous once the collodion membrane peels, followed by a generalized desquamation. The scales gradually grow in size and thickness. Soon after, thick scales cover the whole surface of the animal. The cheeks and lower legs are particularly affected. A thickening of the stratum corneum might result in a slew of other issues. Evaporation may be insufficient as a result of sweat gland malfunction, resulting in hyperthermia. Alopecia areata and potentially dangerous cicatricial alopecia can occur if the scalp is severely affected.

Deep fissures and extremities contractures can also be detected, in addition to the more typically reported undesirable effects. Ectropion can lead to eye dryness (xerophthalmia) and keratitis, which can finally lead to blindness. [21]

### Congenital Ichthyosiform Erythroderma

In the literature, this condition is classified as either bullous or non-bullous congenital ichthyosiform erythroderma. Some publications, however, refer to bullous congenital ichthyosiform erythroderma as epidermolytic ichthyosis. The clinical course is one of the most notable differences between these two clinic kinds. Bullous congenital ichthyosiform erythroderma is characterized by bullous lesions. Furthermore, the bullous type has an autosomal dominant inheritance pattern. Non-bullous congenital ichthyosiform erythroderma, on the other hand, is the most common cause of collodion babies in the literature, this condition is classified as either bullous or non-bullous congenital ichthyosiform erythroderma. Some publications, however, refer to bullous congenital ichthyosiform erythroderma as epidermolytic hyperkeratosis. The clinical course is one of the most notable differences between these two clinic kinds. Bullous congenital ichthyosiform erythroderma is characterized by bullous lesions. Furthermore, the bullous type has an autosomal dominant inheritance pattern. Non-bullous congenital ichthyosiform erythroderma, on the other hand, is the most common cause of collodion babies. [21,8,12,13,6]

The collodion infant membrane exfoliates with time, leaving thin scales that cover the entire body. Thick skin sheets, on the other hand, cannot be likened to the thick, hard scales of lamellar ichthyosis. However, thick sheets, similar to lamellar ichthyosis, can be visible in the temporal region and the lower regions of the legs. It’s also possible that the palmoplantar skin will be affected, resulting in deep cracks. However, generalized erythema is far more common in such instances. Developmental retardation and short structure can be caused by skin barrier malfunction and consequent calorie loss. Hypohidrosis may also occur as a result of sweat gland malfunction. [21]

### Bullous Congenital Ichthyosiform Erythroderma (Epidermolytic Hyperkeratosis)

The occurrence of this clinical picture is influenced by mutations in the keratin 1 and/or 10 genes [12,20]. Large bullous lesions, generalized erythema, and a scaly look may be present at birth in severe cases. Bullous lesions are prone to rupturing, resulting in erosive, erythematous patches on the skin. Bullous lesions are sometimes unpleasant, and as a result, they can be bothersome for an infant in the early stages of life. Diffuse erosive lesions, in particular, pose a high risk of infection. [21]
Harlequin Ichthyosis

The most severe and noticeable kind of ichthyosis is harlequin ichthyosis. These collodion infants are born with thick skin sheets that resemble armour. In addition, the skin is ridged with deep fissures. Because of the loss of skin elasticity, the ears and nose have flattened. The everting of the eyelids and mouth can give this clinical entity a distinct and virtually unique appearance.

Harlequin ichthyosis is an uncommon condition caused by an autosomal recessive gene. The pathophysiology of the condition was revealed to be the result of both structural and functional default of keratin, filaggrin, and the lamellar body in a study of 10 harlequin babies [13,14]. The primary components of stratum corneum include keratin, filaggrin, and lamellar body. In another investigation, protein phosphatase gene mutations linked to serine-treonin protein phosphatase enzyme deficiency on the 11th chromosome were identified as another likely cause of this dangerous condition. [13,14]

History

Hallopeau and Watelet et al. coined the term “collodion Baby” in 1884. Approximately 270 instances or cases have been documented since then. Although different diseases (see table no. 2) and circumstances can cause collodion membrane production, the cause is nearly always an autosomal recessive ichthyosisiform condition.

CASE REPORTS

Collodion baby with dehydration fever : very rare case report

A female neonate born at full term by vaginal delivery to a 26-year-old primigravida mother of a non-consanguineous marriage was admitted to our tertiary care centres’ SNCU with skin dryness, scaling, and fissuring at spots, as well as a fever of 99.4°F for one day. There was no history of drug use, radiation exposure, or any important events during the pregnancy for the mother. [24]

With APGAR scores of 7 and 9, the baby wailed almost immediately after birth. During a medical examination, it was discovered that the entire body was covered in a parchment-like coating (collodion) that was peeling away from the entire body, including the face. There was an outward turning of the mouth.

The potential of sepsis developing early was kept in mind. On a trial-and-error basis, injections of ampicillin/clavulacillin and gentamycin were initiated. After consulting with a dermatologist, liquid paraffin and glycerine were applied to the body three times a day. Eye drops containing ciproflaxacin and carboxymethylcellulose sodium were prescribed for ectropion, and surgical consultation was sought for constriction bands on both hands.

The newborn’s initial sepsis screen was negative (total leukocyte count – 15,000, N53%, L37%), and C-reactive protein (CRP) was negative. Renal function testing revealed hypernatremic dehydration and severe kidney damage. Initial renal function testing revealed elevated BUN levels of 54 mg/dl and creatinine levels of 2.1 mg/dl. With sodium levels of 156 mmol/L, electrolytes revealed hypernatremia. [24]

On the first day of admission, the newborn was given intravenous fluids and antibiotics, and on the second day of admission, she was given expressed breast milk through an orogastric tube. On day two of admission, the fever reduced, and renal function tests improved (BUN – 43 mg/dl and creatinine 1.6), as did sodium levels (150 mmol/l). The skin desquamation was noticed on the fourth day of life. Many bare spots formed from the peeling away of the skin covering at folds and joints. The amount of milk given to each child was gradually increased to 150 ml/kg/day. On the fourth day of admission, a repeat sepsis test was negative after 48 hours. Hypernatremia and acute renal damage both returned to normal levels.

On day 5 of life, the collodion membrane was limited to a small portion of the body due to supportive management and regular skincare, leaving the normal skin behind. On the fifth day of admission, the newborn’s blood culture was sterile, and antibiotics were not given. At two weeks of age, the baby’s skin desquamation was complete, and he was discharged on the fourteenth day of his life. At four weeks of age, a follow-up examination confirmed healthy skin covering and acceptable weight increase. The child is on eye drops for ectropion and is being monitored. The BERA hearing test revealed that the patient’s hearing was normal. The baby was given emollients to apply at home and is now doing well.

Collodion baby with ischemic risk: Treatment by an orthopaedic surgeon

It is the case of an Algerian girl born to nonconsanguineous parents. At 1 minute, 5 minutes, and 10 minutes, the Apgar score was 9/10/10. Bilateral ectropion, echlabium, stenosis of the ear canals, and nasal vestibules were all symptoms of newborn collodion. Collodion membranes were used to wrap the entire body. She was the family’s firstborn child, and there was a familial antecedent in the form of a first-degree cousin of the infant who had the identical birth presentation.
The orthopaedic surgeon was summoned to provide his expert opinion on the hypoperfusion of the fingers and toes. At the time of the clinical evaluation, the hands and feet were wrapped with a flexible membrane without constrictive bands. Vaseline rubs helped to alleviate the hypoperfusion of the extremities.

An interdisciplinary team of dermatologists, ophthalmologists, neonatologists, ENT specialists, physiotherapists, and orthopaedists attended to the newborn in the neonatology department. On day 7, the tiny girl was able to close her mouth and eyes, indicating that she had progressed well. On day 10, the high humidity incubator was turned off. Constrictive bands formed at the root of the fingers and the toes on day 11, producing ischemia. We made the decision to eliminate the ischemia surgically. The membrane was opened like a book and entirely removed under general anaesthetic. The membrane was removed from all of the fingers and toes. The underlying skin appeared to be in good condition. There were no further issues as a result of this.

The baby was fine after the 4-month follow-up. She barely had a few thin membranes left on her back, scalp, axillary hollows, and inguinal folds. The rest of the skin appeared to be in good condition. As a result, this instance is known as “bathing suit ichthyosis.” The TGM1 gene has two mutations, according to genetic tests. This gene is involved in autosomal recessive congenital ichthyosis, particularly the “bathing suit ichthyosis form,” as previously stated. [24]

Case report: Two-day old baby diagnosed by skin biopsy

A 2-day-old male neonate was hospitalized with a complaint of membrane all over his body that had been present from birth. The infant was born on time and was the first child of third-degree consanguineous parents. The whole body was coated with a parchment-like membrane that was peeling off on the chest and abdomen during the examination.

Eversion of the lips, ectropion, flattening of the nose and ears, claw-like hands, and limiting of joint movements were all shown to be associated with the condition. There were no other congenital flaws to be found. Hair and nails were in good condition. The results of routine blood and urine tests were within normal ranges. Epidermal hyperkeratosis and granular layer preservation were found in a skin sample. Intravenous fluids and prophylactic antibiotics were given to the patient in a humidified setting. Emollient was used all over the body. The patient improved after membrane peeling, but the erythroderma remained. The patient was then discharged with instructions to apply emollients on a regular basis and to return for follow-up. [19,24]

Aetiology

Male and female babies both affected, and it affects all populations. This ichthyosis disease diagnosed at time of birth of child and remain continuous throughout life if timely not treated. Desquamation of the collodion membrane is abnormal. It is usually an autosomal recessive, congenital ichthyosis caused by mutations in particular genes (scaly skin condition). However, 10% of collodion newborns have normal underlying skin, which is referred to as a “self-healing” collodion baby [3].

Transmission

CBS is a genetic autosomal recessive disorder. If in any family one child birth with CBS then there are chances of another child also with CBS, if not treated at first baby delivery time. This disease is transmitted genetically from parents to offspring. It just occurs due to error at genetic level i.e. due to mutations at genetic level. Five different genes that also be affected in collodion baby syndrome are CYP4F22, ABCA12, ALOX12B, ALOXE3, NIPAL4 and PNPLA1.

Pathogenesis of Collodion Baby Syndrome

The collodion membrane, like all ichthyosiform disorders, is caused by an epidermal cornification abnormality. Although the aetiology of molecular pathways appears to lead to an epidermal cornification condition, autosomal recessive genetic abnormalities that affect keratinocyte protein and lipid metabolism have also been identified as key cofactors. [23]

Transglutaminase 1 gene mutation (i.e. TGM 1 gene mutation) on 14q11 has been found to be the cause of both autosomal recessive lamellar ichthyosis and congenital ichthyosiform erythroderma (non-bullous). [18,1] Furthermore, distinct molecular pathogenic pathways have been discovered, as well as 5 different gene localizations and more than 50 gene alterations in these genes. [19,17]

Five different genes that also be affected in collodion baby syndrome are CYP4F22, ABCA12, ALOX12B, ALOXE3, NIPAL4 and PNPLA1. And just because of unordered or disordered cornification in the epithelial cells (especially in squamous epithelial cells), many physiological functions like hydration regulation, activity of dendritic cells, desquamation and permeability (i.e. helps to remove toxins and irritants from the body as a result skin remains healthy) fails. [3]

Histopathology of Collodion Baby Syndrome

An eosinophilic, PAS positive stratum corneum accompanied by hyperkeratosis can be seen on light microscopic examination of skin specimens of a newborn child with a collodion membrane in the early periods. The epidermis, on the other hand, is weakened by the granular layer’s thinning. However, in the upper region of the stratum corneum, electron microscopy reveals abundant intracytoplasmic granules and twisted cornocytes. Although there are many lamellar bodies, the intercellular gap and desmosomes are well preserved. The structure of the thinned granular layer is normal. [23]
Diagnosis

The clinical manifestations at the time of birth are used to make the diagnosis. The mutation of the exact gene responsible for the condition can be discovered by genetic testing. A skin punch biopsy is a procedure that involves piercing the targeted gene to indicate the condition of the stratum corneum Sequence in the blood of the infant [17,25]. Collodion infant is a congenital abnormality marked by the presence of a parchment-like or cellophane-like membrane encircling the entire body. Cornification disorder is the cause of this. These babies are frequently born preterm and are only diagnosed at the moment of birth.

Prognosis

The severity and intensity of the sickness determine the lifespan of collodion newborns. Complications such as dehydration, failure to feed, respiratory problems, and septicemia cause the majority of babies to die within the first few days of life. [25] Collodion babies repair themselves within the first few weeks of life. [9]

Clinical Manifestations

The clinical manifestations are given below in the form of table:

<table>
<thead>
<tr>
<th>Serial No.</th>
<th>Human Body System</th>
<th>Clinical Manifestations</th>
</tr>
</thead>
<tbody>
<tr>
<td>01.</td>
<td>Skin</td>
<td>Shiny, Yellow, Parchment-like translucent skin</td>
</tr>
<tr>
<td>02.</td>
<td>Eyes</td>
<td>Ectropion, Conjunctivitis</td>
</tr>
<tr>
<td>03.</td>
<td>Hair</td>
<td>Hypotrichosis (little or no hair growth on the head)</td>
</tr>
<tr>
<td>04.</td>
<td>Mouth</td>
<td>Fish-mouth appearance</td>
</tr>
<tr>
<td>05.</td>
<td>CNS</td>
<td>Neonatal seizures</td>
</tr>
<tr>
<td>06.</td>
<td>Nose</td>
<td>Hypoplastic nasal cartilage, Nose flattening</td>
</tr>
<tr>
<td>07.</td>
<td>Ears</td>
<td>Malformation of pinna, Hypoplastic auricular cartilage</td>
</tr>
<tr>
<td>08.</td>
<td>Other Manifestations</td>
<td>Dehydration, fluid loss, Anal fissures, hypo or hyperthermia</td>
</tr>
</tbody>
</table>

Treatment

Fluid and electrolyte balance, as well as body temperature, must be closely managed in collodion newborns. In addition, the membrane must be lubricated, and appropriate hydration of the skin is one of the most important aspects of treatment in order to achieve elasticity and desquamation. For collodion newborns with ectropion, proper eye care and pain management are required. The management must include humidified incubators and water dressings, as well as emollient agents. If the collodion babies have respiratory failure, ventilator support will almost certainly be required. Antibacterial therapy will be required in cases of epidermolytic hyperkeratosis (bullous congenital ichthyosiform erythroderma) with generalized erythema, bullae, and erosions in addition to conventional therapy. [21] Collodion newborns with wide regions of skin erosion are always at danger of serious infections and even sepsis, hence the best local and systemic antibacterial treatments must be carefully chosen and recommended [3]. Salicylic acid, lactic acid, and propylene glycol are some of the medications that can be used to remove hyperkeratotic sheets from the skin. However, in cases of generalized lesions, especially in infants, it is important to remember that using salicylic acid locally in high dosages can result in salicylic acid toxaemia. As a result, in these circumstances, local remedy should be carefully monitored and carried out in this manner.

Local retinoic acid and calcitriol therapies have been found to be beneficial in collodion newborns with localized lesions [2,16]. Systemic retinoids, which are now the main therapeutic technique in situations of widespread lesions, have been recommended as a viable option. When systemic retinoids were introduced into the practice, fatality rates dropped dramatically. In a trial, acitretin at a dose of 0.5-0.75 mg/kg/day was employed, and the mortality rate of collodion newborns was reduced to 11% (1986) compared to the figures in 1960. (50 percent). Systemic retinoids were started at a dose of 0.5% mg/kg/day in cases of lamellar ichthyosis, and the dose was eventually increased to 2 mg/kg/day. The authors have stated that the extremely thick scales have improved expressively. Congenital ichthyosiform erythroderma has also been proven to benefit from systemic retinoids.
Despite the fact that harlequin foetus is the least common of all the ichthyosiform disorders, it is the most severe. As a result, extremely high mortality rates have been documented. Nonetheless, these rates have decreased in recent years as a result of the introduction of systemic retinoids into clinical practice and the application of improved treatment approaches in intensive care units.

Conclusion:

Pseudoainhum is a disorder that causes a fibrous constrictive ring to form around a limb. These constrictive bands have the potential to cause self-amputation. One of the causes is infant collodion, which has a variety of aetiologies. The physiopathology is poorly understood. The collodion membrane, like all ichthyosiform disorders, is caused by a problem.

In the stratum’s creation, maintenance, and function the skin’s corneum. It’s a condition known as epidermal cornification. For treatment of pseudoainhum, there are no established guidelines. It could be medicinal or surgical in nature. The literature confirms this. Antibiotic prophylaxis is not recommended in a systematic manner. The lubrication and hydration of the joints is the initial treatment. The epidermis This therapy is necessary to maintain the skin’s suppleness and to allow the skin to breathe.

Usually, the baby is taken to a neonatal intensive care facility (NICU). A humidified, temperature-neutral atmosphere is provided by an incubator. Other forms of assistance, such as intravenous fluids and tube feeding, are frequently required. The goal is to maintain the skin supple and minimize scaling. Debridement of the collodion membrane is not recommended (pulled off).

- Regular emollients, such as petrolatum, may be used to maintain the skin moist.
- Anti-inflammatories, such as paracetamol Topical steroid creams to alleviate secondary inflammation
- Artificial tears if ectropion is severe (outward turning eyelid).

A dermatologist and the paediatric team are needed for management. Other professionals who may be required to participate include:

- Ophthalmologist is the first option.
- Genetics expert is the second option.
- Physiotherapist is the third option.

The life expectancy and challenges that a collodion newborn encounters are determined by the underlying disease.

REFERENCES:


