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Diagnostic approach and clinical management in collodion babies: A case report

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Abstract: Collodion baby (CB) is a rare form of congenital ichthyosis, characterized by hyperkeratosis, severe erythroderma, and minimal desquamation. It is a rare condition with a prevalence of one in 300,000 live births and is usually born prematurely. The baby's thick, shiny crust can cause eyelid ectropion, lip deformation, underdeveloped cartilages, and affect the newborn's lung functions, leading to dehydration, malnutrition, hypoxia, and lung infections. The success of the diagnostic approach and clinical management in collodion baby is reported. A 15-hour-old baby girl, J, was born at Fatimah Probolinggo Hospital on July 29, 2024, with tense and blistered skin since birth. She was the second child born by cesarean section with a history of maternal labor. The baby received Vitamin K and Hepatitis B injections shortly after birth. The parents reported a similar complaint in their first child, a collodion baby. After physical examination, laboratory tests, and echocardiography, J was diagnosed with lamellar ichthyosis and ocular ectropion. An echocardiogram was performed on August 2, 2024, and the diagnosis was suspected as collodion syndrome accompanied by extropion oculo dextra sinistra and lamellar ichthyosis. On August 7, 2024, J experienced significant improvement and was discharged from the hospital. A comprehensive approach and treatment from a combination of specialties can improve the prognosis of infants with collodion.

Keywords: *Blistered skin, Clinical management, Collodion baby, Diagnostic approach.*

1. Introduction

Collodion baby (CB) is a rare form of congenital ichthyosis characterized by hyperkeratosis, severe erythroderma and little clinically apparent desquamation. This uncommon clinical condition has an estimated prevalence of one in 300,000 live births. In this condition, the baby is usually born prematurely and is covered by cholodion. Collodion itself is a translucent layer of skin that resembles parchment paper and peels off in the first two to four weeks of life, to reveal various congenital diseases with skin and joint symptoms [1]. Collodion baby (CB) is a rare skin symptom associated with an autosomal inherited disease and mostly occurs in premature infants. At birth, the patient's skin is covered with a thick, taut, shiny, glue-like crust formed by the proliferative stratum corneum. This tension can lead to eyelid ectropion, lip deformation, and underdeveloped nasal and auricular cartilages. It can also affect the sucking and ventilation functions of the newborn's lungs, leading to dehydration, malnutrition, hypoxia and lung infections. It is now thought that some types of autosomal recessive congenital ichthyosis (ARCI) may manifest as CB at birth, and ARCI occurs due to mutations in the ABCA12 gene, ALOX12B, ALOXE3, CASP14, CERS3, CYP4F22, LIPN, NIPAL4/ICHTHYIN, PNPLA1, ALDH3A2, ERCC2/XPD, ABHD5, SDR9C7, SULT2B1, and TGM1 [2]. Recently, Mohamad et al. reported 62 Middle Eastern families from various ethnic backgrounds with ARCI. Pathogenic variants were identified by whole-exome sequencing (WES) in most genes associated with

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ARCI, including TGM1 (21%), CYP4F22 (18%), ALOX12B (14%), ABCA12 (10%), ALOXE3 (6%), NIPAL4 (5%), PNPLA1 (3%), LIPN (2%), and SDR9C7 (2%). Most of the CYP4F22 mutations in the cohort resulted in congenital ichthyosiform erythroderma (Mohamad, 2021). Another recent study reported genetic analysis performed using different sequencing methods, including Sanger sequencing or next-generation sequencing, for 68 patients with a clinical diagnosis of ARCI, including 16 SHCB patients. Most of the causative mutations in the ARCI cohort were found in TGM1 (27.9%), followed by ALOX12B (16.2%), ALOXE3 (14.7%), NIPAL4 (13.2%), ABCA12 (13.2%), PNPLA1 (7.4%), CYP4F22 (5.9%), and SDR9C7 (1.5%). Genetically confirmed SHCB patients showed causative mutations in ALOXE3 (50.0%), ALOX12B (37.5%), PNPLA1 (6.3%), and CYP4F22 (6.3%) [3]. Understanding the genetic and biochemical basis of CB is essential for accurate diagnosis, management, and potentially for the development of targeted therapies. Life expectancy depends on severity and adequate treatment provided.

The age of symptom onset significantly affects prognosis, with rapidly progressive pediatric forms often leading to death. In this study, a 15-hour-old baby girl was referred with a condition where the skin of the whole body looked tense and blister-like since birth, the eyes of the patient also looked pulled so that it was difficult for the baby to close the eyes. After follow-up, the patient was diagnosed with Collodion baby accompanied by Lamellar ichthyosis. The purpose of this study is to understand the clinical manifestations of Collodion Baby and gain knowledge about the condition of Collodion Baby which is a rare condition including its clinical features and diagnostic methods, so that it can be applied to patients in daily practice as a pediatrician.

2. Case Report

J, a 15-hour-old baby girl was referred from RSUD Waluyo Jati Kraksaan to the emergency room of RSUD Dr. Soetomo with the main complaint of tense and blistered skin since birth and diagnosed as collodion baby. Baby JAM was the second child born by SC with a history of maternal labor G2P1000 37/38 weeks + BSC 1x. The baby was born at Fatimah Probolinggo Hospital on July 29, 2024 at 14.00 with a birth weight of 3510 grams, body length 48 cm, head circumference 34 cm, chest circumference 33 cm, APGAR score 8-9 accompanied by skin conditions throughout the body tense and blistering since birth (Figure. 1).

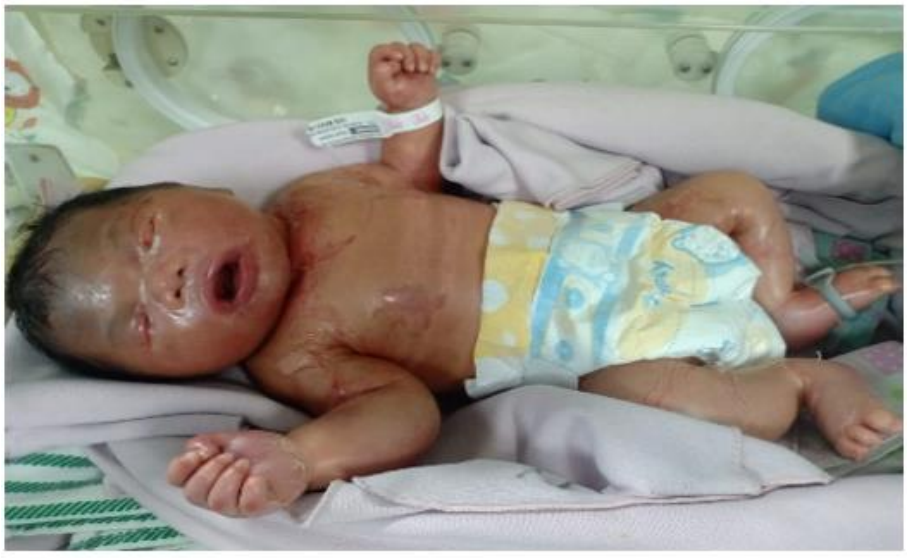

Figure 1.
Condition when the baby is born.

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The baby is also difficult to close the eyes because the upper eyelids and lower eyelids are pulled. There was no temperature instability, no respiratory distress, no jaundice, no cyanosis. The baby has received Vitamin K injection and Hepatitis B injection for dose 0 (given shortly after birth). The baby has not received parenteral care and has not received any drink. The infant had defecated. The patient's parents said that their first child died at the age of 3 days due to a similar complaint (collodion baby). During treatment, the doctor collaborated with colleagues from eye, skin and cardiology to consider the possibility of lamellar ichthyosis, ectropion and cardiac abnormalities if any, but after physical examination, laboratory tests and echocardiography, the laboratory and echochardiography results were within normal range. For eye and skin examination, the patient was diagnosed with lamellar icthyosis and ODS ectropion. There was a family history of the same disease from the patients brother (the first child of the family) (Figure 2).

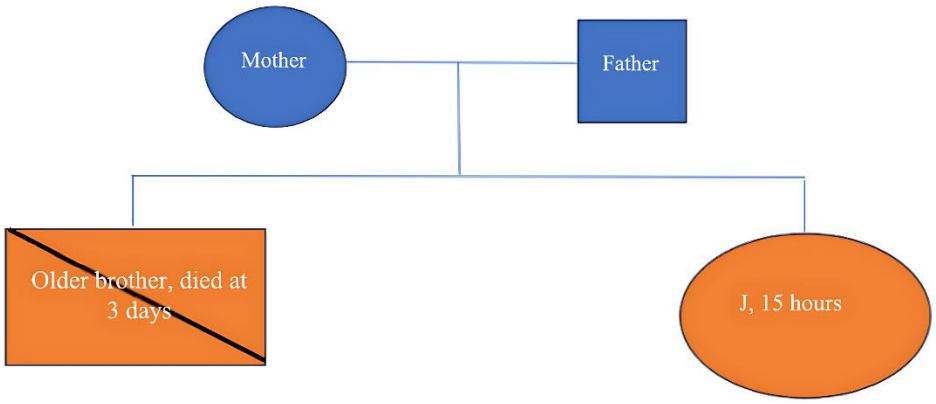

Figure 2.
Pedigree.

The patient underwent a thorough physical examination by a pediatrician. Initially, assessment using the Fenton chart showed that in terms of birth weight, the patient's birth weight was appropriate for gestational age, birth length was appropriate for gestational age, and head circumference was appropriate for gestational age, with all three parameters falling between the 10th precentile and 90th precentile on the Fenton curve (Figure. 3).

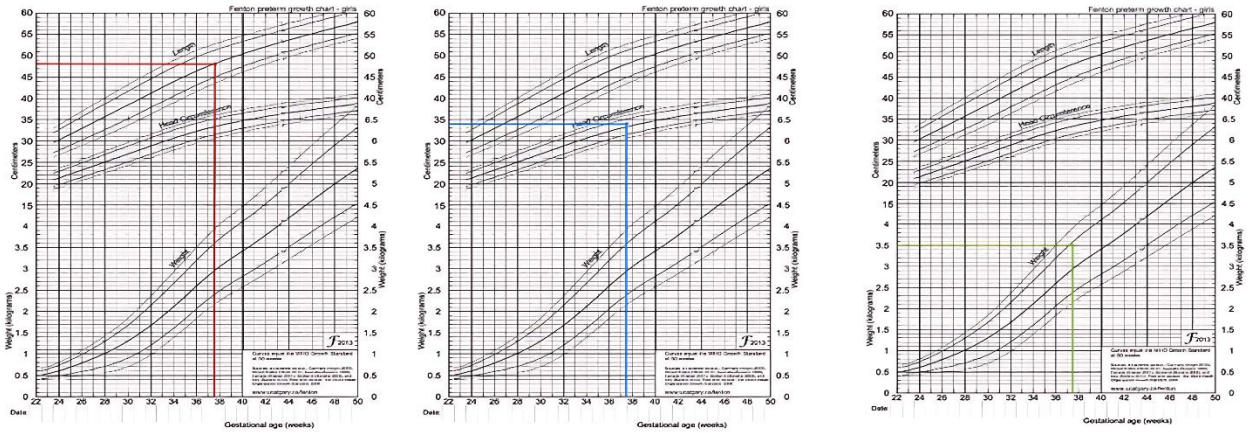

Figure 3.
Fenton chart.

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On general examination performed when first arrived at the emergency room of RSUD Dr. Soetomo Surabaya on July 30, 2024 at 04.27 a.m., the patient came in a conscious state (Glasgow Coma Scale: E4M6V5), the patient's movement was somewhat limited due to icthyosis and the patient's cry was sufficient, with vital signs within the normal range, including a regular heart rate of 152 x/min, a strong and adequate pulse, a respiratory frequency of 56 x/min, a temperature of 36.5°C, and oxygen saturation of 98%. During examination from head to toe, multiple forms of skin abnormalities were seen throughout the body along with erythema and ichthyosis. The head and neck area was not anemic, icteric, cyanosis or dyspnea. Eye examination showed non-pale conjunctiva, non icteric sclera, positive light reflex, pupils that were round and equal to 2 mm in size, and no corneal opacities but the eyes were found to be unable to close properly due to palpebral retraction. In the facial region, there was a transparent paper-like membrane with indistinct borders with an erythematous skin base, and ectropion and eclabium were seen. No enlarged lymph nodes in the neck were detected on palpation. Chest examination revealed symmetrical movement without retraction. Vesicular sounds were present in both lungs, and there were no additional sounds such as rhonki or wheezing in both lung fields.

Heart sounds were normal and regular, with no murmurs or abnormal rhythms. Abdominal examination revealed a convex surface, normal bowel sounds. On the extremities, there was warmth at the acral region, capillary refill time was less than 3 seconds. Examination of the thoracalis anterior et abdominal region and superior et inferior extremities on both dextra and sinistra sides showed multiple transparent membranes, paper-like hyperpigmentation with firm borders, multiple erythematous macules of varying sizes with firm borders and erosions (Figure 4)

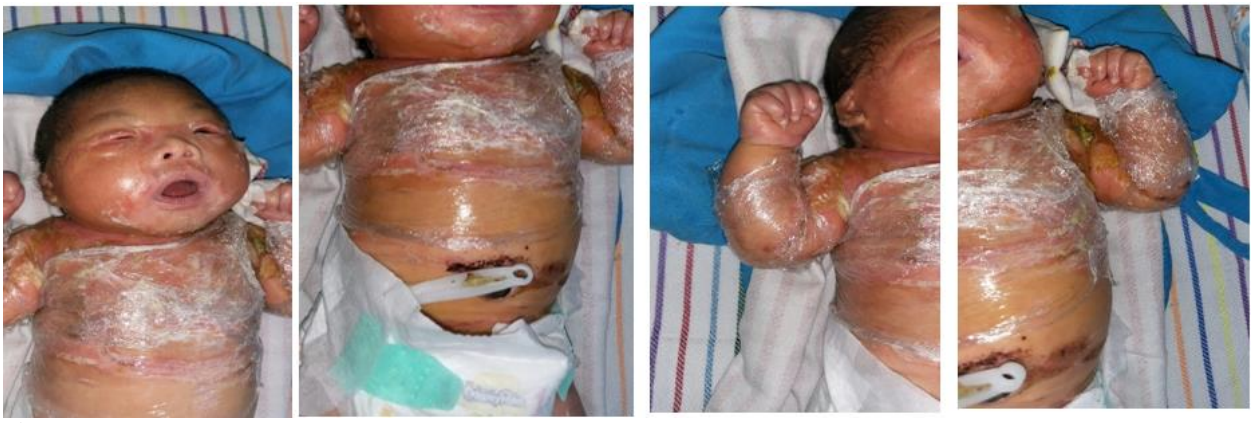

Figure 4.
Clinical features of infants after wrapping to maintain moist skin temperature.

The patient underwent a supporting examination on July 30, 2024, laboratory results showed a hemoglobin level of 16.3 g/dL, hematocrit of 48.0%, leukocyte count of 20,710/µL, and platelet count of 257,000/µL. An echocardiogram was performed on August 2, 2024 and concluded to be normal. Eye examinations were performed periodically from August 1, 2024 until improvement on August 5, 2024 with the same management. Considering the patient's history, physical examination, and supporting examination, the patient's diagnosis was suspected as collodion syndrome baby accompanied by extropion oculo dextra sinistra and lamellar ichthyosis. The therapy given came from various fields, among others:

- The Nutritionist provides nutritional therapy from breast milk and formula milk gradually starting from 312 ml / day on August 01, 2024, 360 ml / day starting from August 2, 2024 to August 4, 2024, 420 ml / day on August 5, 2024, 456 ml / day on August 6, 2024, and gets 480 ml / day on August 7, 2024.

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- The Ophtamology provided NaCl compress therapy, Gentamycin eye ointment 3x1 ODS, cendo lyteers eyedrop 6x1 ODS from August 1, 2024 to August 5, 2024. After the left eyelid has closed and the skin has begun to peel and improve, NaCl compresses are continued, Gentamycin eye ointment 3x1 ODS is replaced with C. polygran eye ointment 3x1 ODS, the duration of Lyteers eyedrop administration is reduced to 4x1 and control to the day eye clinic if the patient is allowed to discharge from hospital.
- The Dermatovenerology provides pseudoceramide cream as often as possible and applied to the whole body and can be given petrolatum jelly if necessary, sodium fusidate cream 2 x 1 on erosive lesions, using moisturizing soap, maintaining skin moisture by putting the baby into a warm incubator, monitoring temperature, hydration and electrolytes, educating the patient's family that the patient's condition may return to normal or may persist, reminding the patient's family to bring the patient to control the skin clinic after hospitalization.
- From the pediatrics itself, the patient was given therapy since July 30, including giving fluids 80 ml / kg / day, breast milk / formula up periodically to 12x23 ml which was increased to 90 ml / kg / day as of July 31, 2024, breast milk / formula up periodically to 12x25 ml, increased again as of August 2 to 110 ml/kg/day with breast milk/formula milk rising periodically to 12x30 ml which was then increased again on August 4, 2024 to 120 ml/kg/day with breast milk/formula milk rising periodically to 12x32 ml which was increased again and maintained as of August 6, 2024 to 150 ml/kg/day with breast milk/formula milk rising periodically to 12x32 ml, Ampicillin injection 175 mg / 12 hours (50 mg / kgbb / times) until August 1, 2024, Gentamicin injection 18 mg / 24 hours (5 mg / kgbb / day) until August 1, 2024. In addition, because on August 7, 2024 the patient had experienced significant improvement, the patient was discharged from hospital and brought home medicines in the form of polygran zalf eyes, artificial tears, pseudoceramide cream, sodium fusidate cream and Paracetamol.

3. Discussion

The female patient was brought to the hospital by her parents because her skin appeared tense and blistered since birth. The parents were also worried that the child would not survive because previously, her first child had similar complaints and died at the age of 3 days. The patient was born via perabdominal delivery with SC, cried immediately after birth, weighed 3,510 grams, and was 48 cm long. The patient had already received Vitamin K injection and Hepatitis B injection for dose 0 (given shortly after birth). No other abnormal conditions were reported other than the apparent skin complaints. Collodion Baby (MPS) is an extremely rare clinical condition, with a prevalence of 1:50,000-100,000 births [4]. It is an autosomal recessive inherited disorder caused by mutations in the adenosine triphosphate-binding A12 gene, which plays an important role in the transport of lipids to the skin surface. It is characterized by the presence of a tight, parchment-like membrane that envelops the entire body at birth, accompanied by generalized scaling of the skin [5]. This membrane plaque puts pediatric patients at high risk of dehydration, thermoregulatory dysfunction and sepsis. In addition, complications such as ectropion, eclabium, and limited joint movement are often observed in colodionized infants due to skin tightness [6]. Patients with CB can be diagnosed by looking at the clinical features shortly after birth. The clinical features of these patients can be seen from the skin, hair, eyes, nose, ears, mouth, extremities, breathing, trunk, central nervous system, and other manifestations which are all summarized in Figure. 5 [7].

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System	Manifestations
Skin	Shiny, yellow, parchment-like taut translucent skin
Hair	Hypotrichosis (little or no hair growth on the head)
Eyes	Ectropion, conjunctivitis
Nose	Flattening of nose, hypoplastic nasal cartilage
Ears	Hypoplastic auricular cartilage
Mouth (lips)	Eclabium (fish-mouth appearance)
Limbs/extremities	Claw-like hands, limitations of joint movements, hypoplastic digits, oedema over the limbs
Respiration	Impaired chest expansion due to tight covering of the chest
Trunk	Peeling of abdomen and chest
CNS	Neonatal seizures
Other manifestations	Anal fissures, dehydration, electrolyte imbalance, fluid loss, hypo- or hyperthermia

Figure 5.
Clinical manifestation of collodion baby syndrome.

In this patient, there was shiny, yellow, parchment-like, translucent skin that was taut, ectropion in both eyes, eclabium (fish-mouth appearance) on the lips and obvious peeling of the skin on the abdomen and chest.

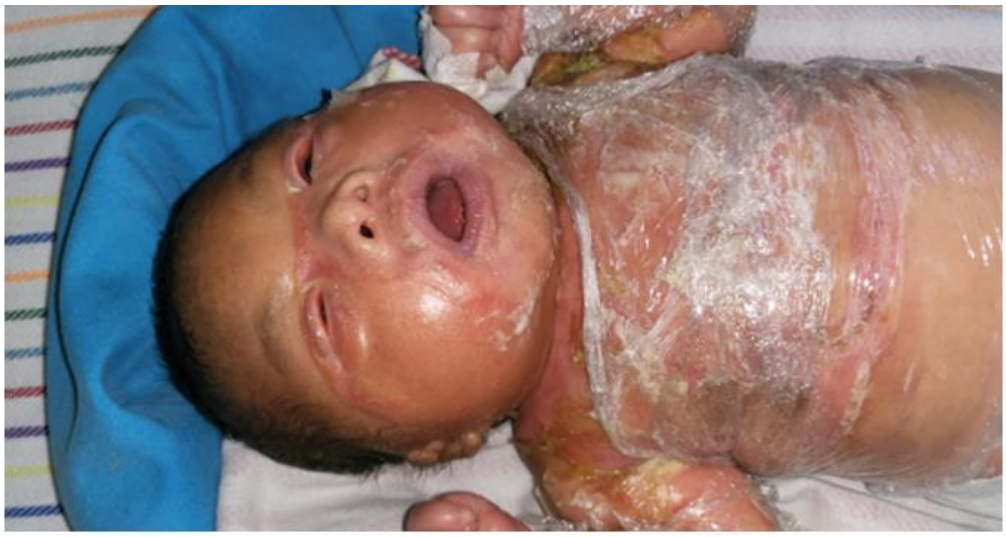

Figure 6.
Patient's clinical manifestation.

During the physical examination performed by the pediatrician, the examination was also assisted by colleagues from ophtamology and dermatovenerology. Encodes the enzyme transglutaminase (Tgase 1) which disrupts the integrity of the layer between the cell membrane and the intercellular matrix, so that its function as a barrier to the passage of body fluids is impaired and results in increased body fluid discharge [8]. Treatment for this condition is to bathe the baby daily and apply a mild emollient such as

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petroleum jelly. Comprehensive care to improve long-term survival involves multidisciplinary pediatricians, dermatologists, ENT specialists, ophthalmologists, plastic surgery care, and physiotherapy [9]. Collodion Baby (CB) is a condition seen in newborns, characterized by a hard, shiny, yellowish, translucent membrane that resembles collodion, commonly called collodion membrane [10]. This membrane develops due to an imbalance of lipid and protein levels in the epidermis. The syndrome stems from erythroderma iktiosiform, a condition primarily associated with baby cholodion. Typically, the disorder affects the entire body, with a stiff appearance similar to parchment or immersion in hot wax [11].

The majority of collodion babies show autosomal recessive erythroderma ichthyosiform, which results from functional mutations in genes such as TGM1, ALOXE3 or ALOX12B, ABCA12, HIPAL4/ichthyin, ABHD5, or other genes related to homeostasis [12]. Although the cause of Collodion Baby syndrome is unknown, it often follows an autosomal recessive inheritance pattern, suggesting a rare link to blood relations. In 10% of cases, collodion babies show normal skin, while the remaining 15% are associated with conditions such as ichthyosis vulgaris, trichotiodystrophy, and metabolic or endocrine disorders that affect keratinization. Tension around the eyes and mouth causes ectropion and eversion of the lips, called Albion, giving it a fish-like appearance with thinning of the nose and ears. If left untreated, this condition can lead to blocked nostrils and, if forcibly opened, can cause keratitis and potential blindness. The stiff skin on the chest can cause breathing difficulties, sometimes resulting in respiratory obstruction. Collodion babies are often born prematurely between 32 and 36 weeks, often with low birth weight, although premature birth itself is not a significant cause. Typically, the collodion membrane begins to dry and slough off within the first 48 hours, and sloughs off completely within 2-4 weeks. The therapeutic strategy for Collodion Baby syndrome is focused on maintaining the skin barrier, managing infection, maintaining fluid and electrolyte balance, and early application of retinoid therapy. Initial treatment involves moisturizers and topical keratolytic agents containing sodium chloride, urea, vitamin E acetate, glycerol and petroleum jelly. However, caution is essential to prevent absorption of topical products and potential toxicity. Hyperkeratotic agents such as lactic acid, glycolic acid, salicylic acid, N-acetyl cystine, and glycols can be used in severe cases. Ectropion is managed with artificial tears and lubricants, with surgery considered in severe cases. Retinoids such as isotretinoin are effective due to their keratolytic effect. Regular cleaning of the external ear canal is essential to prevent crust build-up and reduce the risk of hearing loss. Collodion infants face a higher risk of dehydration and electrolyte imbalance due to increased imperceptible fluid loss through the skin, which requires the use of incubators with high humidity levels, constant temperature monitoring and adequate nutritional support [13]. Aquaphor application has been shown to be effective in reducing transepidermal water loss and lowering the risk of infection. When caring for infants with Collodion Baby Syndrome, it is recommended to perform careful skin care, limit the use of products, and closely observe the potential for infection. The use of topical emollients in the management of Collodion babies is a supportive measure to improve skin health and minimize discomfort. It is an integral part of the overall care plan designed to address the unique challenges associated with this congenital skin disorder.

According to Waghule, et al. [14] the treatment that can be given for this condition is the baby is usually transferred to the neonatal intensive care unit (NICU) using an incubator. Incubators are used because they provide a humidified and neutral temperature environment. Other supportive care in this condition can be given intravenous fluids and tube feeding is often required. The goal of therapy in CB is to keep the skin soft and try to reduce scaling. The collodion membrane should not be dissected (pulled) because it can cause several side effects such as secondary infection, increased risk of fluid and electrolyte loss and interfere with the natural process of shedding. Treatment may include regular emollients such as petrolatum to maintain skin moisture, pain relievers such as paracetamol, mild topical steroids to reduce secondary inflammation and artificial tears if there is severe ectropion (outward eyelid) [14]. Treatment requires the expertise of a dermatologist and a pediatric team. Other specialists who may need to be involved include an Ophthalmologist, Geneticist and Physiotherapist. The life

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expectancy and difficulties faced by a collodion baby depend on the underlying condition. When compared to existing research and theories, this patient has a history of similar disorders in the family, namely from her older sibling. There is no history of consanguineous marriage, no history of maternal complications during pregnancy or exposure to other drugs. The patient is the second child, whose first child died at the age of 3 days due to similar complaints. Complete blood and electrolyte laboratory results are within normal limits. The patient was treated in the HCU and in an incubator to be monitored for body temperature, humidity, and fluid/electrolyte balance and was given antibiotic injections in the form of injections and Gentamicin. The patient was given chloramphenicol eye ointment and artificial tears eye drops for the ectropion she experienced and the patient was given pseudoceramide cream and sodium fusidate for her skin complaints. The patient was still given breast milk and formula every 2 hours during treatment. The patient was in an incubator with a temperature of 30-32 C for seven days until finally allowed to go home with the recommendation to continue to provide emollients regularly and breastfeed.

4. Summary

A 15-hour-old baby girl presented with the chief complaint of taut and blistered skin since birth. The complaint was accompanied by shiny, yellow, parchment-like, translucent skin that was tight, ectropion in both eyes, eclabium (fish-mouth appearance) on the lips and peeling of the abdominal and chest skin that required intensive hospitalization. The patient also seemed to have difficulty moving due to the condition of his skin. Physical examination showed that the patient's birth weight was in accordance with gestational age, birth length was in accordance with gestational age, and head circumference was in accordance with gestational age. On general examination, the patient presented conscious, with limited movement due to icthyosis and vital signs within normal range. During examination from head to toe, multiple forms of skin abnormalities were seen throughout the body along with erythema and icthyosis. The head and neck area was not anemic, icteric, cyanosis or dyspnea. Eye examination revealed eyes that could not close properly due to palpebral retraction. In the facial region, there was a transparent paper-like membrane with indistinct borders with an erythematous skin base, and ectropion and eclabium were seen. Viewed from the thoracalis anterior et abdominal region and superior et inferior extremities both dextra and sinistra side, there was a picture of multiple transparent membranes, paper-like hyperpigmentation with firm boundaries, multiple erythematous macules of various sizes with firm boundaries accompanied by erosion. Therefore, the patient was suspected of Colloidon Baby Syndrome. The patient was treated with nutritional therapy and supportive care. It is a challenging process to make a diagnosis of Colllodion Baby Syndrome as a pediatrician as this condition has a diverse spectrum of clinical manifestations, ranging from milder to severe, which may be influenced by genetic differences among patients. CB is a rare condition that affects multiple systems commonly seen in the skin and eye region of the patient, requiring collaborative efforts for prompt diagnosis. It is important to have a thorough understanding and management of the varied clinical manifestations, by integrating supportive interventions into regular multidisciplinary care. Treatment options such as adequate antibiotic administration for both ocular and skin complaints as well as adequate nutrition, influence the outcome of CB patients. This case report highlights the need to consider CB when a patient presents with shiny, yellow, parchment-like and taut translucent skin accompanied by ectropion in both eyes.

Transparency:

The authors confirm that the manuscript is an honest, accurate, and transparent account of the study; that no vital features of the study have been omitted; and that any discrepancies from the study as planned have been explained. This study followed all ethical practices during writing.

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