Leiner's Disease (Erythroderma Desquamativum) in a Baby Boy

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ABSTRACT

Background: Leiner’s disease (erythroderma desquamativum) is a disorder in infants; it is a complication of seborheic dermatitis with universal and scaly erythema (erythroderma). The case is a baby boy aged 1 month 18 days with white scaly skin for 10 days and fever for 3 days prior to hospital admission. The prognosis is good with the risk of severe infections such as pneumonia, meningitis, and sepsis if not properly treated.

Keywords: Erythroderma desquamativum, infantile seborheic dermatitis, Leiner’s disease

INTRODUCTION

Background

Leiner’s disease or erythroderma desquamativum is a disorder in infants as a complication of seborheic dermatitis with universal and scaly erythema (erythroderma), often followed by secondary bacterial infection. Anemia, diarrhea, and vomiting can be found. The name comes from Karl Leiner, an Austrian pediatrician who discovered a baby with generalized dermatitis with erythematous scales, generalized lymphadenopathy, and diarrhea in 1908.¹²³

Skin manifestations in Leiner’s disease were erythema all over the body and a generalized rough scale accompanied by fever, anemia, diarrhea, vomiting, failure to thrive, and weight loss.⁴ Local or systemic bacterial infections may be recurrent.⁵,⁶,⁷ accompanied with a decreased immune system and possibly lymphadenopathy.⁸,⁹

This disease has many other names, such as Leiner syndrome, C5 complement deficiencies, dermatitis exfoliativa generalized, desquamative erythroderma in infant, eczema universal seborhoeicum, erythroderma desquamativa of Leiner, erythroderma desquamativa in infants, and Leiner Moussous diseases.¹⁰⁻¹²

Epidemiology

Leiner’s disease can occur immediately after birth but more commonly in the first few months (3 weeks – 23 weeks).¹³ It is more common in females and more often among breastfed babies than among formula-fed babies.¹⁴ Another literature mentions that Leiner’s disease most often occurs in the first three months of life with the most susceptible age at 2-12 weeks of age.¹⁵ This disease can appear until in the age of 1.5 years. The association of family members with atopic dermatitis or psoriasis has been studied, but the pattern of heredity remains unclear.¹⁶

Leiner’s disease is a disease caused by primary complement deficiency that can be inherited. The inheritance is autosomal recessive, except for C1 esterase inhibitor deficiency. The incidence is 0.03% in the general population whereas protein C2 deficiency occurs in 1 of 10,000 people.¹⁷ Leiner’s disease is found in fewer than 200,000 people in the United States.¹⁸ Genetic and Rare Disease Information Center (GARD) of the US Department of Health and Human Services (HHS) and the Office of Rare Diseases (ORD) at the National Institutes of Health (NIH) classify Leiner’s disease as a “rare disease”. In Europe, the Consortium of European Partners declares Leiner’s disease as a very rare disease.¹⁹

This disease was more common in the early 1970s and is becoming increasingly rare. The reason remains unknown. Improved hygiene may inhibit the colonization of Malassezia sp., preventing the disease from becoming extensive.²⁰

Etiology

The etiology is idiopathic. Complement system defects have become a major factor in the development of this disease. Defect or deficiency refers to the C5 component of the complement system along with other factors.²¹ In addition to C5 dysfunction, other
possible etiologies include C3, C4, and biotin deficiency.28 Other immune system diseases are also common in infants with Leiner’s disease.1,2,3,4,13

Causes of deficiency in complement components can be primary or secondary ones. The primary cause occurs when there is a disruption of the complement formation pathway caused by the formation of antibodies, while the secondary causes are usually caused by lack of consumption or decreased production of antibody antibodies, such as in the case of malnutrition, disorders at birth, disorders of the liver and kidneys.5,7 This disease is also associated with infection of Malassezia furfur, a lipophilic fungus that colonizes in the sebum-rich skin of newborns, especially in the first month of life. Several studies have shown that Malassezia colonization is more common in infants with infantile seborrheic dermatitis, including atopic dermatitis.16,19

This disease is also often referred to as an extension of seborrheic dermatitis as the typical skin disorder is similar to seborrheic dermatitis. Their differences are that while the etiology of Leiner’s disease remains idiopathic (mostly caused by complement system defects that lead to Malassezia infection), seborrheic dermatitis’ etiology is related to the increased activity of sebaceous glands that also leads to Malassezia infection. Leiner’s disease affects all areas of the body, while seborrheic dermatitis affects hairy areas of the body such as scalp, eyebrows, nasolabial folds, ear canals, back, and chest. Infantile seborrheic dermatitis which usually appears at 3-14 weeks of age but improves spontaneously at 8-12 months of age.10

Pathogenesis
The clinical manifestations of Leiner’s disease are the result of the multifactor interaction of genetic, immune, metabolic, and environmental components, which includes a collection of symptoms of erythroderma, diarrhea, and failure to thrive. Generalized desquamative erythema and dermatitis with reduced body weight are common in breastfed infants due to biotin deficiency.20 Recently, it was found that infants with Leiner’s disease are also more susceptible to infection due to fungal opsonization defects due to deficiency of the C5 Complement component.20

Metabolic and nutritional disturbances are suspected if the baby fails to thrive. Dermatitis initially appears around the mouth, whereas in severe protein malnutrition it can manifest as broad erythema, edema, erosions, and desquamation.20

Malnutrition and zinc deficiency due to low levels of zinc in breast milk can trigger early symptoms. Diarrhea, failure to thrive, and irritability may accompany the dermatitis. Therefore, complete nutritional supplementation such as essential amino acids found in dairy products and vegetable oils is recommended. Breast milk contains less biotin, so breastfed babies will show symptoms earlier than formula-fed babies.20

Erythema in Leiner’s disease is caused by dilatation of blood vessels, resulting in increased blood flow to the skin and increased heat loss. Loss of body heat causes an increase in the basal metabolic rate.1 Basal metabolic rate increase is directly proportional to fluid loss, so the patient tends to become dehydrated. Exfoliated scales on the surface of the skin can cause protein loss and may cause edema.20

Immune System
Complement is a series of circulating enzymatic serum proteins with 9 components, namely C1-C9. The reaction of immunoglobulin (Ig) G or IgM with antigens as part of the immune response activates C1, and then combines with C4 via the classical complement pathway or cascade. The complement then combines with the antigen-antibody complex and undergoes a series of reactions that enhance the immune response against the antigen. This complex process is important in the normal immune response, referred to as complement fixation, which is important in chemotaxis, opsonization (the process of enveloping a pathogenic organism so it can be easily recognized and attacked by the macrophage system), phagocytosis, bacteriolysis, and anaphylactic reactions. Complement deficiency or dysfunction increases the risk of infection and is also

Figure 1. The complement system and complement fixation.7
the keys to CPTHA is probably the most pr yet unknown.3 Clinical characteristics and subsequent headache within seven days Patients with brain injuries may experience infection, central nervous system deficiency, and malfunctions of the phagocyte system, leading to the failure of fungi and bacterial opsonization.1

The most common defect in Leiner’s disease is C5 complement deficiency.22 Sonea, et al, found that patients with Leiner’s disease had a loss of C3 complement, whereas Godyear and Harper found a reduced C4 component with reduced neutrophil mobility in patients with Leiner’s disease.2223 Thus, apart from the defect of C5 complement, C3, C4, or C5 complement dysfunction or deficiency, and hypogammaglobulinemia or other lymphoid system dysfunction may contribute to Leiner’s disease.24

Several family members of one family in Arabia developed meningococcal infection with the absence of serum C5 complement. After investigation, mutations in exon 1 were found, accompanied by a change in cytosine to thymine at position 55 (55C>T) causing a change in the amino acid glutamine at position 19, which gave the stop code for the codon (Q19X), causing the absence of serum C5 complement.25 Three major sequelae of complement deficiencies are: (1) inadequate opsonization; (2) defects in cell lysis; (3) association with other more complex immune system diseases.25

Clinical Manifestations
The skin disorder is generalized erythema and in some parts covered with rough scales. Initially, there are reddish scales on the scalp, face or the area around the mouth, and the gluteal area. These scales spread very quickly to other parts of the body.26

The affected area may become infected and become red and swollen. The baby looks agitated, but it doesn’t cause itching. Other symptoms include diarrhea, systemic infection, central nervous system deficiency, anemia, vomiting, failure to thrive or weight gain, sepsis, lymphadenopathy, and local skin infections.3

The clinical tetrads of Leiner’s disease include generalized erythroderma resembling seborrheic dermatitis, recurrent secondary infection with S. aureus, Candida, or Gram-negative bacteria, persistent malabsorption diarrhea, and failure to thrive.28

Diagnosis
Diagnostic criteria for Leiner’s disease are divided into common and less common criteria. Common ones included clinical tetrad and found opsonization defects of Baker’s yeast and S. aureus, while less common ones included biotin deficiency as evidenced by a significant response to biotin replacement therapy.29

Diagnosis is made based on clinical symptoms. Typical clinical symptoms are reddish seborrhoeic lesions in the scalp, the area around the mouth, and the gluteal region. A distinctive characteristic is a combination of scales and redness. Scalp scales are thick, oily, and sticky, white or yellow in color. Hair can grow on the scales and fall out if the scales fall off. These scales also appear on the hairline up to the eyebrows.1

The histological changes of the skin in Leiner’s disease remain unclear but resemble erythroderma and most closely resemble seborrhoeic dermatitis, which are acanthosis, parakeratosis, hyperkeratosis, papillary edema, and mild lymphocytic infiltration in the epidermis, papillary, and deeper perivascular layers.29

Laboratory tests can be ordered to confirm the diagnosis, which includes measurement of complement levels, immunoglobulin levels, and bacterial cultures.9 Anemia, dysgammaglobulinemia with low IgG and high IgM, and leukocytosis with normal humoral and cellular immunity can be found.20

Differential diagnosis of Leiner’s disease includes infantile seborrhoeic dermatitis, erythroderma, Omenn syndrome, Staphylococcal scalded skin syndrome, toxic shock syndrome, congenital cutaneous candidiasis, ichthyosis, toxic epidermal necrolysis (TEN), Langerhans cell histiocytosis, psoriasis, and atopic dermatitis.28

Treatment
The general objective of therapy is to remove scales and crusts, prevent the development of fungal colonization, prevent secondary infection, and reduce erythema.20 This disease has the potential to cause death because of the systemic effects caused by immune system deficiency.20

The main treatment must include regular monitoring of vital signs, fluid and electrolyte balance, prevention of hyperpyrexia, administration of moisturizers to maintain the skin barrier, hydration, administration of topical steroids; systemic antibiotics is recommended if there is a secondary bacterial infection. The family must be educated on these therapeutic modalities.29

Adequate nutrition is also essential. Biotin, a water-soluble vitamin in foods such as milk, egg yolks, kidneys, and liver, can help in curing Leiner’s disease.2227 In familial Leiner’s disease, fresh frozen plasma and whole blood can be given to treat complement deficiency.8

The recommended topical therapy for Leiner’s disease is open wet dressing and emollient with or without low or very low potency corticosteroid ointment. Topical corticosteroids of moderate or high potency may be applied to lichenified areas and not for long-term use.13 Topical antibiotics may be given concurrently with emollients to treat superimposed infections.22 Systemic steroids are indicated if the erythroderma does not subside even after improvement in nutritional status and control of infection, with initial dose of prednisone 1 to 2 mg/kg/day and a maintenance dose of 0.5 mg/kg/day. Dose tapering must be considered because relapse may occur.28

Plasma therapy is indicated if: (1) a complete immunologic evaluation including examination of cell-mediated immunity has been performed, (2) is considered only after cell-mediated or humoral immunity deficiency has been excluded, (3) functional C5 or C3 deficiency is most likely the diagnosis, (4) the use of plasma therapy with caution in children with recurrent infection, and (5) any fresh blood products should be prioritized for children suspected of having an immunologic deficiency disorder.28
Scalp
Scalp therapy with 3% salicylic acid in olive oil or water solvent, olive oil compresses, and a weak potency topical corticosteroid (1% hydrocortisone cream or lotion) for several days followed by imidazole topical antifungal (2% ketoconazole cream or lotion or shampoo) ketoconazole 1%, gentle baby shampoo, skin care, and moisturizer.1

Intertriginous Area
Clioquinol 0.2%-0.5% in zinc lotion or zinc oil may be applied. If there is a secondary infection such as candidiasis, apply nystatin or amphotericin B lotion or cream. In wet areas, apply 0.1%-0.25% gentian violet with a cotton swab. Imidazole preparations (2% ketoconazole) in the form of a paste, cream, or lotion may be effective.1

Prognosis
The prognosis for this disease is good if treated properly. There is a risk of severe infections such as pneumonia, meningitis, and sepsis.1,3,5

CASE
A baby boy aged 1 month 18 days (weight 3200 grams, body length 53 cm) was admitted to H. Boejasin Pelaihari Hospital with reddish scaly body skin for 10 days prior to admission. Initially, the scales appear on the scalp and face and then spread throughout the body. The scales are thick, oily, sticky, and yellowish-white in color. Constant fever was found for 3 days prior to hospital admission. Other complaints such as itching, diarrhea, vomiting, weakness, seizures, and decreased consciousness were denied. The patient has still breastfed since birth.

He was born spontaneously with the help of a midwife, at 36 weeks of gestational age, with a birth weight of 2500 grams, a body length of 51 cm, and cried immediately. The mother had no complaints during the pregnancy but never had ANC or ultrasound examinations. No past medical history or family history of related disease.

Generalized erythematous macules were found with yellowish-white, thin to thick lamellar to pityriasisiform scales all over the body (mostly on the face, around the eyes), sizes of various sizes, confluent, irregular edges, and well-decamarated. The skin feels rough and dries (Figure 2).

Laboratory findings were moderate anemia (hemoglobin 9.5 g/dL), leukocytosis (leukocytes 12,500/μL), and lymphocytosis (lymphocytes 6,000/μL).

The patient was diagnosed with Leiner's disease based on clinical symptoms, which are reddish seborrheic lesions (thick, oily, and sticky, white or yellow scales from lamellar to pityriasisform) and redness all over the patient's body.1

The other diagnostic criteria for Leiner's disease are divided into common and less common. The common criteria include clinical tetrad (generalized erythroderma resembling seborrheic dermatitis, recurrent secondary infection with S. aureus, Candida, or Gram-negative bacteria, persistent malabsorption diarrhea, and failure to thrive) and opsonization defects of Baker's yeast and S. aureus, while the less common one includes dysfunction as evidenced by the significant response to biotin replacement therapy.28 This patient has generalized erythroderma resembling seborrheic dermatitis, secondary infection and failure to thrive as common criteria and assumption of biotin deficiency often occurred in breastfed babies, as the less common criteria.

Laboratory examination of Leiner's disease may demonstrate anemia, dysgammaglobulinemia with low IgG and high IgM, and leukocytosis with normal humoral and cellular immunity.28 Moderate anemia (hemoglobin 9.5 g/dL) and leukocytosis (leukocytes 12,500/μL) in this patient may aid in the diagnosis.

The patient received a DSIVNS infusion of 8 drops per minute intravenously (micro), cefotaxime 150 mg/8 hours iv, bolus desamethasone iv 1.5 mg continued with 3 x 0.5 mg iv, probiotics (Lactobacillus acidophilus, Lactobacillus salivarius, Bifidobacterium lactis, Bifidobacterium longum, Bifidobacterium infantis, Lactobacillus casei, and Lactococcus lactis) 1 x 1 gram, zinc syrup 1 x 10 mg, NaCl dressing before topical application of 3% salicylic acid ointment, lanolin, 0.1% betamethasone valerate, and vaseline album 2 twice daily (morning-evening) thinly applied, and 2% miconazole cream 2 twice daily.

Figure 2. A) Generalized erythematous macules were seen with lamellar to pityriasisform scales with a combination of thick and thin scales all over the patient’s face and chest. B) Generalized erythematous macular rash with rough scales on the abdomen to the patient’s lower extremities.
The patient was discharged on the 5th day of treatment with probiotics (Lactobacillus acidophilus, Lactobacillus salivarius, Bifidobacterium lactis, Bifidobacterium longum, Bifidobacterium infantis, Lactobacillus casei, and Lactococcus lactis) 1 x 1 gram, 1x10 mg zinc syrup, 3% salicylic acid ointment, lanolin, betamethasone valerate 0.1%, and vaseline cream twice daily (morning-evening) on the whole body.

DISCUSSION

Leiner's disease can occur at birth but more often develops in the first few months of a baby's life (3–23 weeks), and is more common in breastfed infants than in formula-fed infants due to biotin deficiency.13,14 This corresponds to the patient's age of 1 month 18 days and receiving only breast milk.

The patient's weight is 3200 grams and his length is 53 cm, and according to WHO standards, the patient has failure to thrive, defined as a condition of delayed physical growth in infants and children, failure to gain weight in accordance with a normal growth chart, compared to body length.23 This is in accordance with the symptoms of Leiner's disease.8

The patient's family complained of the patient's scaly skin for approximately 10 days, on the scalp and face and then spreading throughout the body, and constant fever since about 3 days prior to hospital admission.

On examination of the lesion, generalized erythematous macules were found with varying scales (famellar to pytiriasiform), thin to thick, yellowish-white in color throughout the body, multiple with varying sizes, confluent, irregular edges, and decamarated borders. In Leiner's disease, skin abnormalities that can be found are universal erythema, while in some parts they are covered with rough scales. Initially, there are reddish scales on the scalp, face or the area around the mouth, and the gluteal area.6 Erythema in Leiner's disease is caused by the dilation of blood vessels, which increases blood flow to the skin and increases heat loss, which causes an increase in the basal metabolic rate which is directly proportional to fluid loss.20

The clinical manifestations of Leiner's disease are the result of the multifactor interaction of genetic, immune, metabolic, and environmental components, which includes a collection of symptoms of erythroderma, diaper rash, and failure to thrive.32

Leiner's disease can be distinguished from infantile seborrhoeic dermatitis which usually appears at 3-14 weeks of age but improves spontaneously at 8-12 months of age. Infantile seborrhoeic dermatitis may present as an early form of Leiner's disease. Other differential diagnoses, such as psoriasis, are ruled out because of the presence of decamarated erythematous patches with coarse scales, white or silver-colored layers, and transparent like mica with wax drop phenomenon, Auspitz, and Koebner.

Anemia and leukocytosis in this patient can be triggered either by failure to thrive or infection. The complement and immunoglobulin tests were not carried out due to limited facilities.

On histopathological examination, the histological changes of the skin in Leiner's disease remain unclear, but resemble erythroderma and most closely resemble seborrhoeic dermatitis; it consists of acanthosis, parakeratosis, hyperkeratosis, papillary edema, and mild lymphocytic infiltration in the epidermis, papillary and deeper perivascular layers.28 No histopathological examination was performed on this patient due to limited facilities.

Treatment of Leiner's disease includes; regular monitoring of vital signs, fluid and electrolyte balance, prevention of hyperpyrexia, moisturizers to maintain the skin barrier, hydration, topical steroids, transfusion of PRC for anemia, and systemic antibiotics for secondary bacterial infection is present.20

Adequate nutrition is also essential. Biotin, a water-soluble vitamin in foods such as milk, egg yolks, kidneys, and liver, can help in curing Leiner's disease.20,27 In familial Leiner's disease, fresh frozen plasma and whole blood can be administered to treat complement deficiency.8

The recommended topical therapy for Leiner's disease is open wet dressing and emollient with or without low or very low potency corticosteroid ointment. Topical corticosteroids of moderate or high potency may be applied to lichenified areas and not for long-term use.15 Topical antibiotics may be given concurrently with emollients to treat superimposed infections.22 Systemic steroids are indicated if the erythroderma does not subside even after improvement in nutritional status and control of infection, with prednisone initial dose of 1 to 2 mg/kg/day and a maintenance dose of 0.5 mg/kg/day. Dose tapering must be considered because relapse may occur.22

Scalp therapy with salicylic acid 3% in olive oil or water solvent, olive oil compresses, and a weak potency topical corticosteroid (1% hydrocortisone cream or lotion) for several days followed by topical imidazole (ketoconazole 2% cream or lotion or ketoconazole 1% shampoo), gentle baby shampoo, skincare and moisturizer.1 Clioquinol 0.2%–0.5% in zinc lotion or zinc oil can be given in intertriginous area. For secondary candidiasis, apply nystatin or amphotericin B lotion or cream. In wet areas, apply 0.1%–0.25% gentian violet with a cotton swab.1
Conclusion

Diagnosis of Leiner’s disease can be based on history and physical examination. Typical clinical symptoms are generalized erythema and rough scales throughout the body, accompanied by anemia and failure to thrive. First-line therapy is to replace fluid loss, body temperature maintenance, moisturizers to maintain the skin barrier, hydration, topical steroids, and systemic antibiotics for secondary bacterial infection.

REFERENCES