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Case Report

A Case Report: Beneficial Effect of Powder Human Milk in an Infant with Bartter Syndrome

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Abstract

Introduction: Bartter Syndrome (BS) is a genetic kidney disorder that can be diagnosed at birth and affects 1 in 1,000,000 inhabitants. BS is characterized by losses of minerals such as sodium, potassium, or chloride through urine. This disease considers five different subtypes that are determined by the site of mutation in the gene. Patients with BS must have adequate medical treatment in addition to emphasizing the importance of a diet that supports the restitution of minerals lost due to the disease.

Case: We present the case of a 21-month-old female infant diagnosed with disorders resulting from renal tubular function, heart murmur, severe protein-calorie malnutrition with frequent dehydration, and Bartter syndrome type III. At the beginning of her consultations, the patient weighed 2.86 kg, length of 52 cm and the following biochemical evaluation: platelets 439,500/µl (142,000-424,000), urea 124 mg/dl (15-39), serum creatinine 0.31 mg/dl (0.50-1.20), phosphorus 5.1 mg/dl (2.7-4.5), serum calcium 12.5 mg/dl (8.4-10.2), chlorine 68 mmol/l (98-107), potassium 3.04 mmol/l (3.50-5.10) and sodium 146 mmol/l (135-145). The patient was fed comfort milk formula + powdered human milk, as a result, her weight and length increased (4.56 kg and 62 cm). The results of the biochemical evaluation were: platelets 229,600/µl (142,000-424,000), urea 96 mg/dl (15-39), serum creatinine 1.3 mg/dl (0.50-1.20), phosphorus 4.1 mg/dl (2.7-4.5), serum calcium 11.4 mg/dl (8.4-10.2), chlorine 86 mmol/l (98-107), potassium 2.9 mmol/l (3.50-5.10) and sodium 136 mmol/l (135-145).

Conclusion: BS is a pathological entity that causes multiple alterations at the renal, hydro electrolytic, hemodynamic, nutritional, and developmental levels, in addition to leading to frequent hospital stays. Feeding powdered human milk can be part of the dietary strategy for this type of patient.

Keywords: *Bartter Syndrome; Human Milk Powder; Milk Formula; Dehydration;Diet*

Abbreviations

A/G: Albumin Globulin Ratio; AGAP: Anion Gap; Alb: Albumin; ALP: Alkaline Phosphatase; BCG: Calmette-Guerin Bacillus (Tuberculosis Vaccine); BE: Base Excess; BS: Bartter Syndrome; BSND: Barttin CLCNK Type Accessory Subunit Beta; BUN: Blood Urea Nitrogen; Ca: Calcium; Cl: Chloride; CLCNKA: Chloride Voltage-Gated Channel Ka; CLCNKB: Chloride Voltage-Gated Channel Kb; CREA: Creatinine; D Bile: Direct Bilirubin; ESRD: End-Stage Renal Disease; Glob: Globulin; Glu: Glucose; GPT: Pyruvate Transaminase Test; HCO: Bicarbonate Ion Level in the Blood; HTC: Hematocrit Level in the Blood; K: Potassium; LDH: Lactate Dehydrogenase Enzyme Test; Leu: Leukocytes; LFT: Liver Function Tests; Lymph: Lymphocytes; Na: Sodium; NDI: Nephrogenic Diabetes Insipidus; Neu: Neutrophils; NSAIDs: Non-Steroidal Anti-Inflammatory Drugs; P: Phosphate; PaO_2: Partial Pressure of Oxygen in Blood; PCO_2: Partial Pressure of Carbon Dioxide in the Blood; PGE2: Prostaglandin E2; pH: Potential of Hydrogen; A Measure of Acidity or Alkalinity; PHM: Powder Human Milk; PO: "Per Os"; Taken Orally; ROMK: Renal Outer Medullary Potassium Channel; SET: Serum Electrolytes Test; SGPT: Serum Glutamic Pyruvic Transaminase; TAL: Thick Ascending Limb; T Bile: Total Bilirubin; TGO: Oxaloacetic Transaminase Test; TP: Total Proteins

Introduction

Bartter syndrome (BS) is a genetic kidney disorder that affects 1 in every 1,000,000 people worldwide. BS is caused by defective salt reabsorption in the thick ascending limb (TAL) of the loop of Henle that is characterized by losses of minerals (sodium, potassium, chloride) through urine [1,2]. BS comprises a group of tubulopathies that present with hypokalemia, metabolic alkalosis, hyperreninemia and hyperaldosteronism, growth retardation, frequent dehydration, and normal blood pressure [3].

Cunha and Heilberg described the symptoms that usually occur in the different subtypes of BS that exist [1]. BS Type I: Presents from birth with severe salt losses, hyposthenuria, increased renal production of prostaglandin E2 (PGE2), and growth retardation. If patients suffering from this type of BS are not treated, this pathology can cause death. BS Type II: Also called the prenatal variant of BS, because it causes prematurity at birth. Other symptoms described are: the production of proteins that lose their function, rapidly eliminating the ROMK protein, polyhydramnios, nephrocalcinosis, hypokalemia, alkalosis, hyposthenuria, and transient hyperkalemia. SB Type III: symptoms appear during childhood presenting hypokalemia, hypochloremic alkalosis, salt loss, polyuria, and delayed growth of the infant. They usually present hypochloremia, which is very serious if it occurs in this type of BS. Another condition of this variant that, although very rare, is nephrocalcinosis [1]. There are three variants of BS Type III: neonatal BS, prenatal BS, and the Gitelma phenotype. BS Type IV with two variants, IVa caused by mutations in the BSND gene and IVb by mutations in the CLCNKA and CLCNKB genes, causing deafness, impairment in the functioning of chloride channels, polyhydramnios, prematurity, hypokalemia, defect in the concentration of and induces nephrogenic diabetes insipidus (NDI), as well as growth retardation and end-stage renal disease (ESRD). BS Type V is characterized by autosomal dominant hypo calcemic hypercalciuria (calcium loss) [1].

The objective of treatment for these types of BS focuses on reducing the loss of fluids and electrolytes that are caused by the dehydration characteristic of the disease. Taking sodium, potassium, or magnesium supplements helps a faster recovery, combined with rehydration with isotonic saline solutions. Other basic medications for adequate treatment are prostaglandin inhibitors, spironolactone, angiotensin-converting enzyme inhibitors, vitamins A, C, D, and E, propranolol, and non-steroidal anti-inflammatory drugs (NSAIDs) that help improve tubulopathies [2,4].

Patients with BS require pharmacological treatment aimed at acid-base and hydro electrolyte balance disorders. They must receive adequate nutrition with dietary strategies to compensate for the loss of minerals in addition to the arrest of their growth and development. To counteract sodium and chloride losses, it is advisable to administer a diet with salt (salty foods or salt supplements). The diet is supplemented with sodium chloride tablets for non-prolonged periods, since degenerative diseases may appear [5]. In the case of hypokalemia, a diet rich in fruits, vegetables, meats, poultry, and fish is ideal due to its high potassium content. Dietary carbohydrates help insulin secretion by promoting its absorption. For hypomagnesemia and hypocalciuria, a diet rich in legumes, beef, nuts, green

leafy vegetables, seeds, bananas, whole grains, dark chocolate, and fish are recommended as sources of magnesium and calcium [5]. These feeding strategies are feasible in the case of teething infants and older patients; however, it is mostly difficult in younger infants. Therefore, breast milk substitutes are used in neonates. In this case, powdered human milk (PHM) was used, which preserves the high biological value of its proteins. These proteins are more easily absorbed and digested with less alteration at the kidney level. In addition, PHM contains other bioactive components that improve mineral stabilization. Consequently, it results in greater weight and height gain with an expected increase in the growth and development of infants. Thus, PHM provides benefits, particularly to patients with BS.

Therefore, this report aims to raise awareness of the beneficial potential that results from feeding powdered human milk to infants with BS disease.

Case Report

Birth

Female patient, third pregnancy of a 27-year-old mother (G3P1C0A1) with ingestion of substances of abuse since she was 14 years of age. He was born vaginally at 36 weeks of gestation, weight and length at birth 2.00 kg/48 cm. The patient was classified as a newborn with low birth weight (LBW) and low weight for gestational age, head circumference, APGAR, and Silverman values unknown (Figure 1 and 2). She was fed formula from birth and occasionally breast milk. Incomplete vaccination schedule, only including BCG, hepatitis B, hexavalent, and pneumococcus.

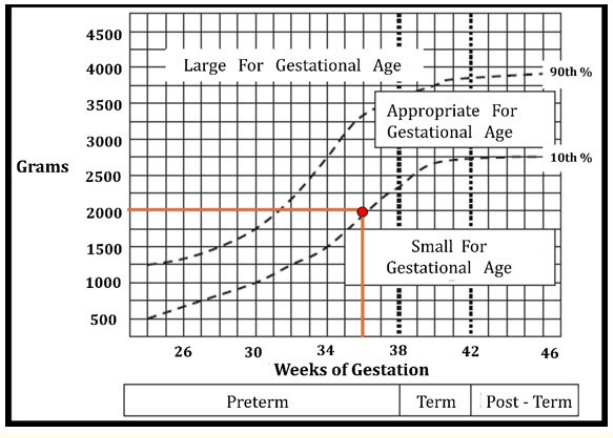


Figure 1: *Birth weight in relation to gestational week, the point marks the position where the patient with SB was at birth [6].*

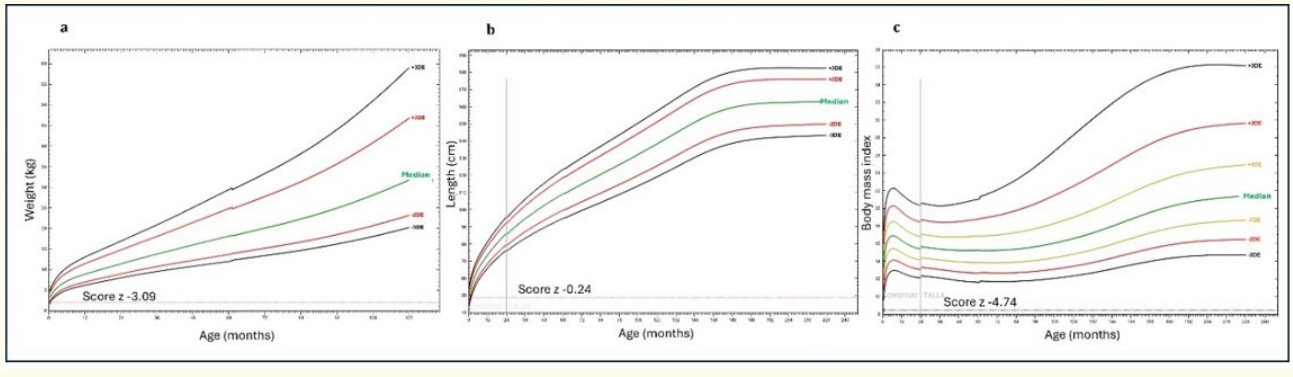


Figure 2: *Weight-Length-BMI at 0 months of age (a) Weight/age (b) Length/age (c) Body mass index/age.*

Seven months old

The patient was admitted to the Nephrology-Pediatrics service for the first time due to fever, vomiting, and diarrhea. At the time of admission, he was diagnosed with severe malnutrition and stunted height, hypernatremic-hyperosmolar dehydration, urinary tract infection, and WHO grade II hypochromic microcytic anemia (Figure 3). Upon admission to the hospital, she was reported with a fever of 38.5 °C after the application of the rotavirus and pneumococcus vaccine. Subsequently, she begins with vomiting, diarrhea with stools up to 5 times in 24 hours without mucus or blood, and dehydration. The patient registers a weight of 2.86 kg (ideal for age 7.57 kg, ideal for length 3.8 kg) and a length of 52 cm (ideal for age 66.8 cm). The biochemical evaluation reported: platelets 439,500/µl (142,000-424,000), urea 124 mg/dl (15-39), serum creatinine 0.31 mg/dl (0.50-1.20), phosphorus 5.1 mg/dl (2.7-4.5), serum calcium 12.5 mg/dl (8.4-10.2), chloride 68 mmol/l (98-107), potassium 3.04 mmol/l (3.50-5.10) and sodium 146 mmol/l (135-145). She was administered paracetamol, hydrated, and fed with 60 ml every 3 h of starter milk formula, supplemented with vitamins A, C, and D (400 IU PO every 24h, 1 ml), vitamin E (25 IU PO every 24h) and ferrous sulfate (8 mg PO every 24h).

Figure 3: *Patient with SB hospitalized at 7 months of age.*

At 7 months 13 days, an improvement in her dehydration and a continuous increase in weight was observed in the patient 3.06 kg (ideal for age 7.60 kg, ideal for length 4.20 kg), length 53.8 cm (ideal for age 67.3 cm) so she was discharged and it was suggested that she continue with the same home nutritional intake, considering for her discharge diagnosis: disorders resulting from renal tubular function, heart murmur and Bartter syndrome (Figure 4).

Figure 4: *Patient with SB about to leave the hospital at 7 months of age.*

Twelve months old

At 12 months and 17 days, the patient's weight decreased (3.0 kg) (Figure 5), so feeding with formula for premature babies was started, 6 feedings of 2-3 oz every 4 hours, achieving only a slight increase in weight (Figure 6).

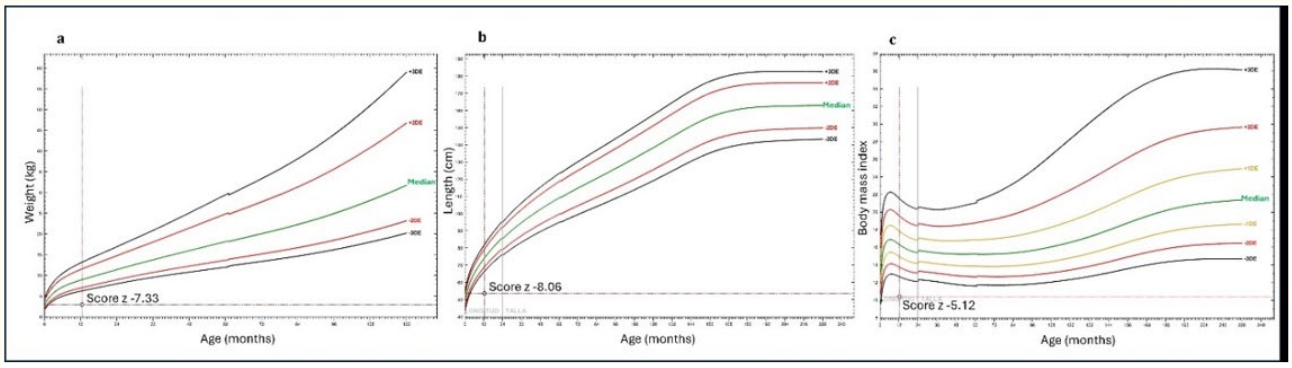


Figure 5: *Weight-length-BMI at 12 months of age (a) Weight/age (b) Length/age (c) Body mass index/age.*

Figure 6: *Patient with SB at 12 months of age.*

Fifteen months old

At 15 months of age, she was admitted to the hospital again due to bilateral basal wheezing, so nebulized treatment was indicated with immediate improvement. Subsequently, it was suspended to avoid potassium imbalance based on the analysis results, pH 7.5 (7.35-7.45), PCO_2 35 kPa/mmHg (35-48), PO_2 80 kPa/mmHg (25-45), HTC 24% (37.7-53.7), sodium 139.90 mmol/l (135-145), potassium 2.40 mmol/l (3.50 -5.10), HCO 34.6 mmol/l (22-29), AGAP 14.5 mEq/l (8-12) and BE 12.7 (+2.3/-2.3) (Figure 7).

The patient initially remained fasting. When she showed clinical improvement, complementary feeding was started for her age, which she tolerated appropriately. In the analyzes carried out, she presented the following blood chemistry results: Glu 64 mg/dl (60-125),

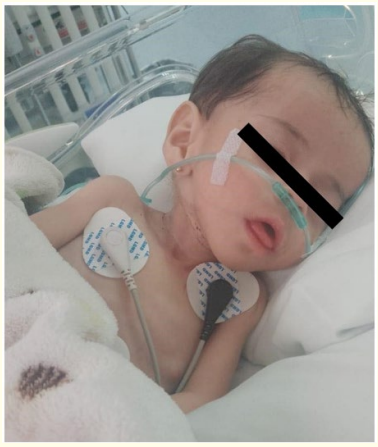


Figure 7: *Patient with SB hospitalized at 15 months of age.*

urea 184 mg/dl (15-39), BUN 86 mg/dl (6.00-20.00) and CREA 2.05 mg/dl (0.50-1.20); SET: phosphorus 7.1 mmol/l (2.7-4.5), calcium 10.9 mmol/l (8.4-10.2), chloride 83 mmol/l (98-107), potassium 2.80 mmol/l (3.50-5.10) and sodium 141 mmol/l (135-145); LFT: total cholesterol 292 mg/dl (100-200), TBil 0.50 mg/dl (0.1-1.2), D Bile 0.10 mg/dl (0-0.3), TP 9.40 mg/dl (6.3-7.9), Alb 5.53 mg /dl (3.5-5.0), Glob 3.87 mg/dl (0.8-1.4) TGO 20 U/l (6-34), SGPT 77 U/l (7-35), ALP 268 IU/l (40-129), LDH 385 mg/dl (60.00 - 140.00), Leu 7.30% (4.60 - 10.20), Neu 42.2% (37-80) and Lymph 47.1% (10-50).

In addition, during her hospitalization, intravenous fluids were replaced, which improved her hydration status and clinical condition in general, so it was decided to discharge him with recommendations on warning signs regarding Bartter syndrome and an appointment was made with Pediatric Nephrology for follow-up. The Pediatric Clinical Nutrition service, after the evaluation, indicated that the patient received starter formula, 8 feedings of 3 oz + 2 oz of pasteurized human milk (from human milk bank) + module (honey) due to her severe and exacerbated protein-calorie malnutrition (Figure 8). With this nutrition plan, the patient managed to increase her weight in less time, 3,480 kg (ideal for length 4.80 kg, ideal for age 5.1 kg) and 54 cm in length (ideal for age 73.4 cm) (Figure 9).

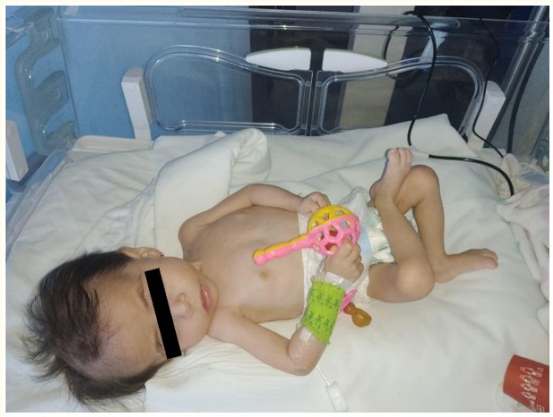


Figure 8: *Patient with SB about to leave the hospital at 15 months of age.*

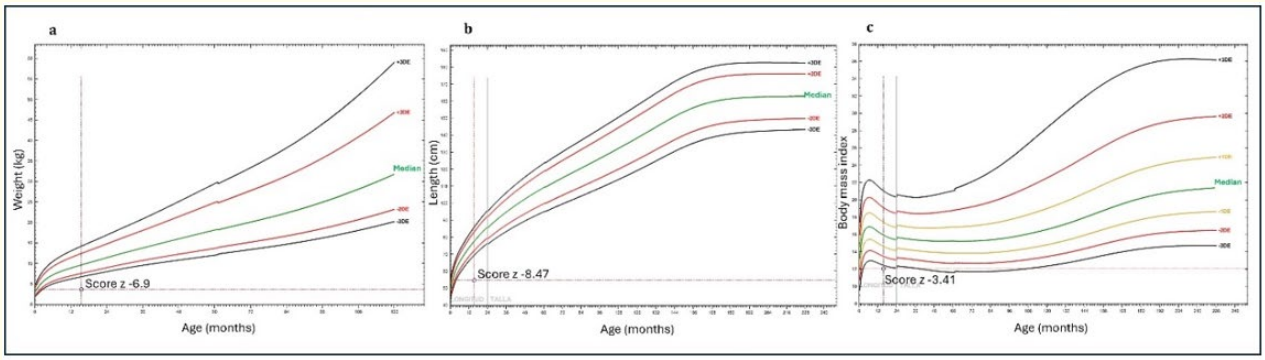


Figure 9: *Weight-length-BMI at 15 months of age (a) Weight/age (b) Length/age (c) Body mass index/age.*

Seventeen months old

At 17 months of age (Figure 10) the patient was started with comfort formula (13 oz) + powdered human milk (9 oz) that was donated by the human milk research laboratory. At that time, the patient registered a weight of 3.68 kg (ideal for length 5.0 kg, ideal for age 9.6 kg) and 57.2 cm in length (ideal for age 79.7 cm) (Figure 11).

Figure 10: *Patient with SB at 17 months of age.*

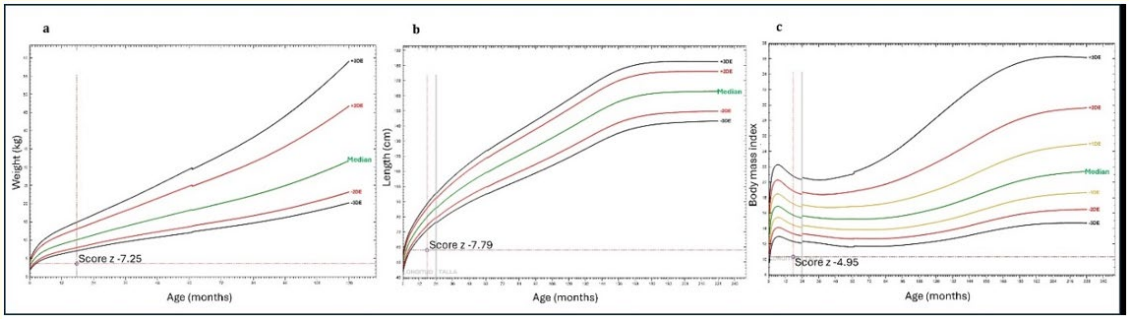


Figure 11: *Weight-length-BMI at 17 months of age (a) Weight/age (b) Length/age (c) Body mass index/age.*

When evaluating the weight gain at 18 months (Figure 12), the patient was recommended to continue with the same initial diet of comfort formula (16 oz) and powdered human milk (9 oz). At this stage, the patient recorded a weight of 3.70 kg (ideal for length 5.4 kg, ideal for age 10.2 kg) and 58 cm in length (ideal for age 80.7 cm) (Figure 13).

Figure 12: *Patient with SB at 18 months of age.*

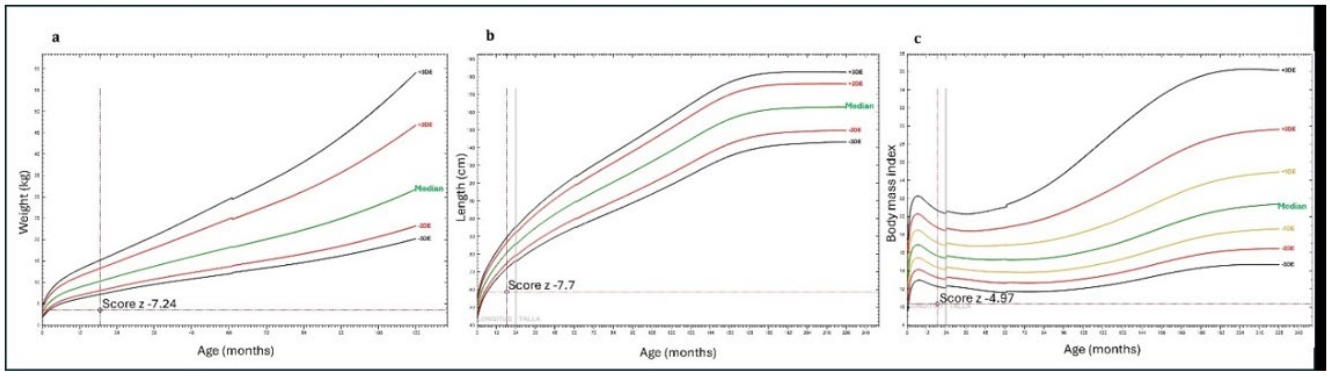


Figure 13: *Weight-Length-BMI at 18 months of age (a) Weight/age (b) Length/age (c) Body mass index/age.*

Twenty months old

Three months after feeding with powdered human milk and complementary feeding, the patient showed an increase in weight and length, 4.56 kg and 62 cm respectively (Figure 14). In this evaluation, an increase in muscle strength was observed, which generated greater activity (ability to hold her head and sit alone) (Figure 15). In addition, there was an improvement in the results of the biochemical evaluation: platelets 229,600/µl (142,000-424,000), urea 96 mg/dl (15-39), serum creatinine 1.3 mg/dl (0.50-1.20), phosphorus 4.1 mg/dl (2.7-4.5), serum calcium 11.4 mg/dl (8.4-10.2), chloride 86 mmol/l (98-107), potassium 2.9 mmol/l (3.50-5.10) and sodium 136 mmol/l (135-145).

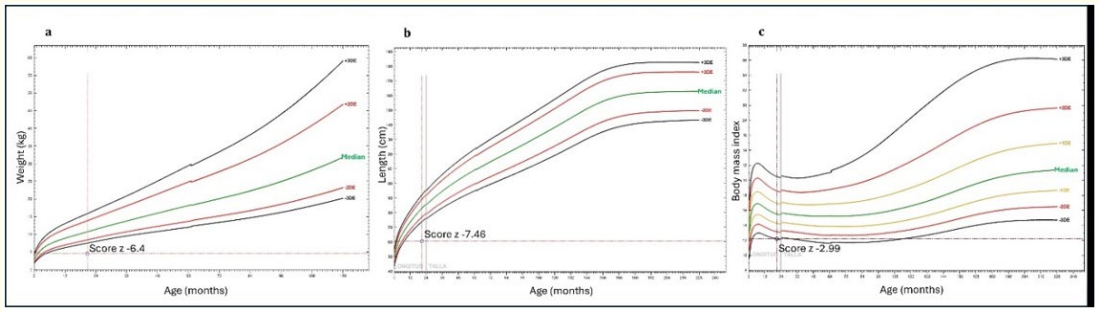


Figure 14: *Weight-length-BMI at 20 months of age (a) Weight/age (b) Length/age (c) Body mass index/age.*

Figure 15: *Patient with SB at 20 months and 11 days of age.*

Discussion

In this case, the patient was diagnosed with BS which, due to its characteristics, is classified as a type III variant; however, the diagnosis is established at 7 months of extrauterine life, which leads to severe malnutrition with a risk of delay in neuromotor and neurobehavioral development. Therefore, medical treatment and restoring growth with the best nutritional strategy were established as priority objectives.

The ideal food for a lactating human being is its own mother's milk, however, this is not always possible for multiple reasons. In this situation, it is necessary to turn to other alternatives, always considering the best of them. In the logical order, if it is not possible to breastfeed with your own mother's milk, the second alternative should always be human milk, either pasteurized bank milk or, as in this case, powdered human milk, and ultimately, the milk substitutes or their hydrolysates, modular or master formulas with the high socioeconomic and health impact that the latter implies.

Human milk powder is a product obtained from the spray drying process. During the procedure, feed flow, the inlet temperature of drying air, and the drying gas temperature are controlled. The adequate manipulation of the above features is combined to minimize the loss of nutrients and immunological factors contained in the milk, allowing its conservation for a longer time.

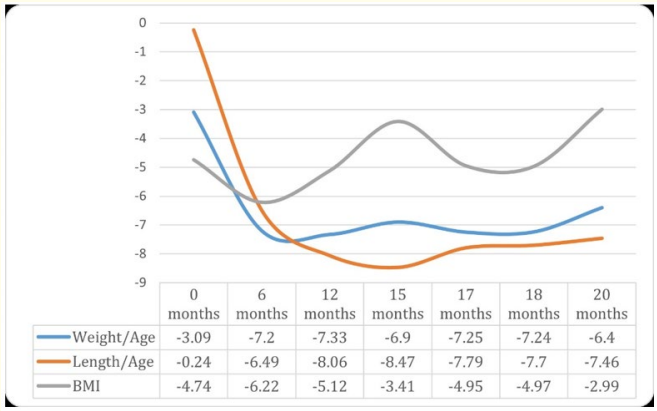
Human milk has a particular aminogram since its proteins have different functions in the digestion process, which are active in the human gastrointestinal tract. Lönnerdal describes in two investigations the benefit of human milk proteins when consumed by the infant

[7,8]. Lipases aid lipid digestion in premature infants; amylase helps the digestion of complex carbohydrates; α_1-antitrypsin limits the activity of pancreatic enzymes, acting as a brake molecule; β-casein forms bonds with Ca, facilitating its absorption; lactoferrin is an iron-binding protein; haptocorrin binds vitamins B12; α-lactalbumin, which is found in greater quantities in human milk, helps the absorption of minerals, and finally, immunoglobulins help the immune system against pathogenic bacteria, viruses and yeasts [7].

For all of the above, the ideal food for an infant is human milk directly from the mother's breast, failing that, freshly expressed human milk, or in adverse circumstances, banked human milk. It is important to emphasize that applying heat treatment at high temperatures to human milk denatures some proteins and destroys lipase activity. Therefore, it is important that during the pasteurization of liquid human milk, the temperature is controlled to avoid protein denaturation. This effect occurs less frequently when applying the spray drying technique to obtain powdered human milk.

Infants with SB suffer losses of sodium, potassium, magnesium, and chloride that can lead to severe dehydration in addition to severe growth retardation. For this reason, early diagnosis, timely medical treatment, and a correct diet that recovers or supports short-stature growth are essential. In this patient, medical treatment was administered after diagnosis, and feeding with milk substitutes was started with unfavorable results. Subsequently, she was fed with banked human milk and finally, with powdered human milk with encouraging results in her growth and development.

Powdered human milk contains a high concentration of nutrients that include growth factors, pre- and probiotics, immunological substances, hormones, enzymes, and immunoprotective cells, which make it a complete food for infants, helping to retain sodium, potassium, and chlorine, increasing weight and size significantly and improving their quality of life (Figure 16).



	0 months	6 months	12 months	15 months	17 months	18 months	20 months
Weight/Age	-3.09	-7.2	-7.33	-6.9	-7.25	-7.24	-6.4
Length/Age	-0.24	-6.49	-8.06	-8.47	-7.79	-7.7	-7.46
BMI	-4.74	-6.22	-5.12	-3.41	-4.95	-4.97	-2.99

Figure 16: *Growth parameters from 0 to 20 months of age.*

Conclusion

BS is a pathological entity that causes multiple alterations at the renal, hydro electrolytic, hemodynamic, nutritional, and developmental levels, in addition to causing frequent and long hospital stays. If an early diagnosis is achieved, timely medical treatment is established and an adequate nutritional strategy is provided, the prognosis for life and biological function is good. Feeding with powdered human milk can be part of the correct feeding strategy in this type of patient considering that its bioactive factors will impact the physiology of digestion, metabolism, and excretion and on the metabolic programming of the first 1000 days in the life of a human being.

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Conflict of Interest

The authors declare that they have no conflict of interest.

Informed Consent Statement

This study was also approved by the Ethical Research Committee 08 June 2022, with registration number HCG/CEI-0907/22 and research registration 141/22.

Bibliography

1. CunhaTdS., *et al*. "Bartter syndrome: Causes, diagnosis, and treatment". *International Journal of Nephrology and Renovascular Disease* 11 (2018): 291-301.
2. Nascimento CLP., *et al*. "Treatment of Bartter syndrome. Unsolved issue". *Jornal de Pediatria* 90.5 (2014): 512-517.
3. López-Pérez JJ., *et al*. "Síndrome de Bartter. Reporte de un caso y revisión de la literatura". *Revista Med* 19.2 (2011): 185-206.
4. Vaisbich MH., *et al*. "Bartter syndrome: Benefits and side effects of long-term treatment". *Pediatric Nephrology* 19.8 (2004): 858-863.
5. Francini F., *et al*. "The dietary approach to the treatment of the rare genetic tubulopathies Gitelman's and Bartter's syndromes". *Nutrients* 13.9 (2021): 2960.
6. William A., *et al*. "A recommendation for the definition of 'late preterm' (near-term) and the birth weight gestational age classification system". *Seminars in Perinatology* 30.1 (2006): 2-7.
7. Lönnerdal B. "Bioactive proteins in human milk: Mechanisms of action". *The Journal of Pediatrics* 156.2 (2010): S26-S30.
8. Lönnerdal B. "Nutritional and physiologic significance of human milk proteins". *The American Journal of Clinical Nutrition* 77.6 (2003): 1537-1543.

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