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Short Bowel Syndrome: A Case Series and Review of Literature

Kısa Barsak Sendromu: Olgu Serisi ve Literatür Derlemesi

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ABSTRACT
Short Bowel Syndrome, defined as remaining small bowel in continuity of less than 200 cm, is a disorder with varied presentations and frequent and often difficult-to-manage complications. The most commonly encountered complications are mainly nutritional, gastrointestinal and nephrological. Anticoagulation and bone disorders due to micronutrient and drug malabsorption, among other causes, are also encountered. The clinical follow-ups and considerations necessary vary between patients. Functional, pathophysiological, etiological, clinical and anatomical classifications exist to help physicians predict the required interventions. Herein, we summarise our experience with three cases with differing presentations and prognoses. We discuss the problems encountered during their management in light of the existing literature and guidelines. Specialised units and a multi-departmental approach remain vital in managing intestinal failure and short bowel syndrome; better tools and further research are yet to be required.
Keywords: Catheter-related infections, home parenteral nutrition, sepsis

ÖZ
İnce bağırsağın 200 cm'den daha az devamlılıkta kalması olarak tanımlanan Kısa Bağırsak Sendromu, çeşitli prezentasyonlara sahip, sık görülen ve sıklıkla tedavisi zor komplikasyonlarla seyreden bir hastalıktır. En sık karşılaşılan komplikasyonlar temel olarak beslenme, gastrointestinal ve nefrolojiktir. Diğer sebeplerin yanı sıra mikrobesin ve ilaç malabsorbsiyonuna bağlı antikoagülasyon ve kemik bozukluklarıyla da karşılaşılmaktadır. Klinik takipler ve gerekli hususlar hastalar arasında farklılık gösterir. Hekimlerin gerekli müdahaleleri tahmin etmelerine yardımcı olmak için fonksiyonel, patofizyolojik, etiyolojik, klinik ve anatomik sınıflandırmalar mevcuttur. Burada farklı sunum ve prognozlara sahip üç vakayla ilgili deneyimlerimizin bir özetini sunuyoruz. Yönetimi sırasında karşılaşılan sorunları mevcut literatür ve kılavuzlar ışığında tartışıyoruz. Bağırsak yetmezliği ve kısa bağırsak sendromu vakalarının tedavisinde özel birimler ve çok bölümlü yaklaşım hala hayati önem taşır ve daha iyi araçlara ve daha fazla araştırmaya ihtiyaç mevcuttur.
Anahtar Kelimeler: Evde parenteral besleme, kateter kaynaklı enfeksiyonlar, sepsis

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INTRODUCTION

Intestinal failure (IF) is defined as gut function below the minimal amount necessary for absorption of macronutrients and/or electrolytes to the point of requiring intravenous intervention in order to continue health and growth. Intestinal insufficiency is defined as a gut function reduction that does not require any intravenous (IV) intervention for continued health and/or growth.[1]

The remaining small bowel in continuity of less than 200 cm is defined as short bowel syndrome (SBS). In adults, short bowel syndrome is usually caused by surgical resections due to Crohn's disease, malignancy, radiation or vascular insufficiency.[2]

IF is classified under five categories: functional classification (type 1 acute and short-term conditions, type 2 prolonged acute conditions, and type 3 potentially chronic conditions), pathophysiological classification (short bowel, intestinal fistula, intestinal dysmotility, mechanical obstruction, and extensive small bowel mucosal disease), etiological classification (severe GI or systemic benign diseases and end-stage intra-abdominal or pelvic cancer), clinical classification (based on requirements for energy and the volume of IV supplementation), anatomical classification (end-jejunostomy with no colon in continuity, jejunocolic anastomosis with no ileocecal valve and a part of the colon in continuity, and jejunoileal

anastomosis with both the ileocecal valve and the entire colon in continuity). Patients with irreversible IF will require long-term or lifelong home parenteral nutrition (HPN) or intestinal transplantation.[3]

In this presentation, we aimed to present 3 cases diagnosed with Short Bowel Syndrome that we followed up with three differing presentations and prognoses.

CASES

A signed informed consent in accordance with international guidelines was obtained from all cases presented herein.

CASE 1

A 46-year-old female patient was admitted to the emergency department 11 years ago with abdominal pain. After evaluation, she was diagnosed with mesenteric thrombosis and underwent a jejunostomy, leaving 50 cm of small intestine from the ligament of Treitz (subtotal small intestine resection + right hemicolectomy + Hartman procedure). For 11 years, she was followed and treated with HPN with Type 3 chronic intestinal insufficiency. The left half of the transverse colon, descending colon, and sigmoid colon are healthy but not functional. There was no feature in her medical history other than the use of oral contraceptives. No features have been identified in her family history and habits. No features other than jejunostomy were detected in her physical examination. The thrombophilia panel was evaluated as normal.

Adaptation Period: In the postoperative period, the patient was treated with oral fluid restriction of 1.5 litres, a short bowel diet, IV proton pump inhibitors, and IV glutamine. With Abound™ (Abbott) and Modulen™ (Nestle) treatments as an oral nutrition supplement, the jejunostomy discharge of 5 litres decreased to 2.5 litres. Olive oil-based parenteral nutrition treatment was started at 25 kcal/kg/day. The fluid deficit was met by calculating the jejunostomy discharge and the insensible loss. IV solutions were used for trace elements and vitamins.

Chronic Period: As home parenteral nutrition treatment, multi-chamber bag parenteral nutrition preparation, parenteral fluid and vitamin replacement are administered by the patient daily and infused overnight. Follow-ups are weekly. Upon admission postoperatively, the patient weighed 64 kg (BMI: 28.4). Still, weight loss developed, and she is being followed at 35 kg (BMI: 15.5). Clinical follow-up revealed that oral intake did not contribute to caloric intake. Vitamin C and selenium levels were low, while vitamin A, E, zinc, copper and chromium levels were normal.

Follow-up Process: She was hospitalised 68 times during the 11-year follow-up period. 45 hospitalisations were due to infectious reasons, and 23 were non-infectious.

Complication Management: She was admitted 41 times due to catheter infections (one of which was ICU), twice for upper respiratory infection, once for urinary tract infections and once for acute cholangitis. She was admitted twice for acute kidney injury, nine times for supportive treatment, twice for port care, once for hemoptysis, twice for anaemia, three times for elevated liver enzymes, once for suspected pulmonary embolism, once for cholecystitis, once for severe hyperkalemia, once for elevated CRP for a total of 23 non-infectious admissions. Hypokalemia and hypomagnesemia were the most commonly detected electrolyte imbalances. It was determined that she had disrupted her diet with hyperosmolar fluid (fruit juice). Spironolactone tablets were initiated to control hypokalemia, and her potassium levels stabilised around 3-3.5. Vitamin K deficiency developed two years after diagnosis. Despite no elevation of INR, excessive bleeding was noted during her catheter insertions. Three ampoules of vitamin K were replaced intravenously annually. No further bleeding complications occurred. In nephrological evaluation, although the patient presents with intermittent AKI, eGFR is 85 ml/min. In osteoporosis evaluation, femur T score – 2.5, lumbar vertebra – 2.8 was determined. Vitamin D supplements were administered IM.

CASE 2

A 54-year-old male patient was admitted to the emergency department seven years ago with abdominal pain and was diagnosed with portal and mesenteric vein thrombosis. He underwent subtotal small intestine and right colon resection, 50 cm from Treitz, and a jejuno-colic anastomosis (transverse colon) operation. He has been followed with enteral nutrition for seven years without the need for parenteral support treatment. His medical history includes hypertension and lower extremity superficial thrombophlebitis one year before the date of the event. No characteristics were noted in his family history and habits. On physical examination, there is no feature except a surgical scar in the abdomen. In the etiological evaluation, he was diagnosed with thrombophilia panel positivity (MTHFR gene mutation and PAI serpine 1 gene heterozygous mutation) and Behçet's disease (HLA B51 positive). Intestinal failure was considered as Type 3 chronic intestinal failure. Abdominal ultrasonography revealed portal vein thrombosis, an infarct area in the right posterior liver, and splenomegaly. The patient was initiated on methylprednisolone, azathioprine, warfarin and ramipril.

Adaptation Period: Nutritional therapy was arranged as short bowel diet regulation at 30 kcal/kg/

day, oral fluid restriction, oral vitamin supplement, oral proton pump inhibitor, and loperamide. However, the patient could not reach sufficient calories during daily nutritional monitoring. Therefore, Abound™, Modulen™, Fortimel Compact Protein™ and Fortimel Energy™ 1.5 kcal were started as oral nutrition products for the patient. The patient's weight loss was controlled with 40 kcal/kg/day treatment. The frequency of defecation became stable at thrice per day.

Chronic Period: The patient, who weighed 94 kg (BMI: 29.65) preoperatively, weighed 84 kg (BMI: 26.5) at the outpatient clinic follow-up. After seven years of follow-ups, his weight is currently 72 kg (BMI: 22.7).

Follow-up process*:* He was hospitalised twice for parenteral support treatment due to weight loss but was unsuccessful due to upper extremity brachial vein thrombosis in both hospitalisations. Vitamin B12 deficiency developed and was replaced intramuscularly following inadequate response to sublingual replacement. Vitamin D deficiency was replaced with IM. Oral vitamin and micronutrient support was given. For magnesium deficiency, oral magnesium preparations were used twice a day. Due to the anaemia, treatment with IV iron preparations was needed four times.

Complication Management: Gastrointestinal complications: The patient's diarrhea was followed at 3-4 times daily. Whenever the patient disrupted his diet, the complaints of dyspepsia, tenesmus and diarrhea increased. They were controlled with diet regulation, pancreatic enzyme and ursodeoxycholic acid. In the 6th month, gallbladder stones were detected and are being monitored without complications. His diet was revised due to calcium oxalate crystals in the urine. Regarding micronutrients, after six months of follow-up, vitamin B12 and vitamin D were found insufficient and were replaced with IM. After muscle cramps, magnesium deficiency was detected and controlled with oral magnesium twice daily. Iron deficiency developed and treated with IV iron therapy. Low levels of selenium, copper, vitamin C and vitamin A are treated with a multivitamin preparation containing oral trace elements twice daily. Under warfarin, half a tablet/day, the INR levels remained between 1.5 and 3.5. During this period, dose regulations were required. Once his INR level was detected above 10 and the patient presented with hematuria, it was managed with dose regulation without additional complications. Diet regulations and fibre changes within the nutritional products affect the patient's warfarin dose. In nephrological evaluation, eGFR is monitored at 105 ml/min. Intermittent laboratory findings of INR above 4 cause hematuria attacks and, alongside the concurrent calcium oxalate crystals, cause associated renal colic complaints. No stones were detected. No osteopenia was detected at osteoporosis follow-ups.

CASE 3

A 65-year-old female patient with a history of cholecystectomy, sleeve gastrectomy, previous tongue cancer (and radiotherapy), COPD, coronary artery disease, paroxysmal atrial fibrillation, pulmonary hypertension, and chronic renal failure presented three years ago with abdominal pain. She was admitted to the emergency clinic and, with the diagnosis of mesenteric ischemia, underwent small bowel resection, leaving 40 cm from Treitz, and a right hemicolectomy was performed, including the right half of the transverse colon. The patient was followed with parenteral nutrition for four months, then underwent STEP operation and jejunocolic anastomosis. She has been followed up with chronic intestinal failure for the last three years.

Adaptation Period: Following jejunostomy and right colon hemicolectomy surgery, she was followed with parenteral nutrition. For two months postoperatively, she was managed as an inpatient, with varying hyper-hypovolemia, IV proton pump inhibitors, oral fluid restriction, short bowel diet, and one catheter infection. STEP surgery was performed after two months. During the adaptation period after STEP surgery, oral proton pump inhibitors, ursodeoxycholic acid, and pancreatic enzymes were added to her treatment and were beneficial for her dyspeptic complaints. Due to radiotherapy, oral intake was impaired due to insufficient saliva secretion and lack of teeth. She could not tolerate glutamine, Abound™ and additional nutritional support products. Oral calories consumed ranged between 1500 kcal/day and 2200 kcal/day. The protein and calorie intake of the diet was increased. Since the patient had a sleeve gastrectomy in the past, bromelain was used for protein digestion to no benefit.

Chronic Period and Follow-Up Process: Home health care units monitored the patient at home. She was admitted intermittently for anaemia for approximately six weeks and once due to acute kidney injury. The need for parenteral nutrition remained very limited after STEP surgery, and the need for fluid and electrolyte support bi-weekly continued. Parenteral nutrition and IV vitamin support are needed for three days every 2-3 weeks.

A bone marrow biopsy was performed to examine the aetiology of anemia, and erythropoietin treatment was started upon detection of myelodysplasia. The patient no longer needs blood transfusions. The genetic thrombophilia panel was evaluated as normal.

Complication Management: Nephrologically, eGFR is monitored at 30 ml/min and Creatinine at 1.7 mg/dl. Gastrointestinal complications include com-

plaints of dyspepsia and diarrhea. Defecation is controlled at 3-4 times daily with proton pump inhibitors, pancreatic enzyme, ursodeoxycholic acid and diet management. Difficulty swallowing, absence of teeth, previous sleeve gastrectomy and cholecystectomy restrict oral calorie and fluid intake. She also experiences frequent hypervolemia-hypovolemia problems and hypo-hypertensive attacks due to cardiorenal problems. The patient, whose weight was 83 kg (BMI: 34.5) preoperatively and 69 kg (BMI: 28.8) postoperatively, is currently being followed at 61 kg (BMI: 25.4). Oral intake support is managed by dietary regulations and high protein liquid food intake. The patient doesn't consume nutritional products. Citrulline levels were normal. B12 deficiency is treated intramuscularly. Oral multivitamin tablets, folic acid, oral zinc and magnesium supplements are needed twice daily. During follow-ups, copper and selenium levels were low. The fluid requirement is 5 litres every 14 days and is provided peripherally with diuretic treatment. Potassium levels vary between 3-3.5. There is borderline hypophosphatemia (2,4). Albumin levels are monitored as 2.9 g/dl. Osteoporosis: During her follow-ups, osteoporosis was detected in 2020. IM Vitamin D replacement was initiated. IV osteoporosis treatment is planned.

DISCUSSION AND CONCLUSION

In adults, SBS is a special clinical condition that requires follow-up and treatment by units specialised in the management of nutrition and complications that develop after massive intestinal surgery. Management of nutritional therapy begins in the postoperative period and varies depending on the location and length of intestinal resection. This case series discusses the management of macronutrient and micronutrient deficiencies and their complications and medications.

The cases defined are Case 1; type 3, benign aetiology, end jejunostomy, clinically classified as PN1 and FE3, an adult case with no additional disease, Case 2; type 3, benign aetiology, jejunocolic anastomosis (no ileocecal valve), an adult case with known hypertension and Behçet's disease, Case 3; type 3, benign aetiology, STEP and jejunocolic anastomosis (no ileocecal valve), clinically classified as PN1 and FE1, adult and with previous diagnoses of tongue cancer (radiotherapy), hypertension, COPD, CKD, diastolic heart failure, paroxysmal atrial fibrillation, sleeve gastrectomy and cholecystectomy.

In the postoperative period, an intestinal rehabilitation program is needed to increase the function of the remaining intestine, minimise the need for parenteral nutrition and liquid electrolytes, and prevent complications. In this adaptation process (6 months-2 years), glutamine, enteral nutrition, modified diet, growth factors (GLP-2 agonist), growth hormone, octreotide, proton pump inhibitors and loperamide treatments have been used.[4] The ESPEN Guide evaluates these recommendations more clearly.[1] In all of our cases, a diet high in complex carbohydrates and protein and low in fat was recommended during the adaptation period. Fluid intake was restricted. Glutamine, PPI, loperamide, and polymeric products (primarily high in MCT) were used. A decrease in the number and amount of defecation (including stoma exit) was achieved in all cases. Enteral supplement products with high MCT content couldn't be continued long-term due to intolerance and were continued with polymeric products. Although dietary compliance deteriorated in the long term, the number of defecations did not increase.

For the nutritional treatment of cases with short bowel syndrome, enteral and parenteral nutrition, liquid electrolyte replacement, and vitamin and trace element replacement needs should be evaluated and planned according to the patient's short bowel classifications.[5] While case 1 was followed up with an olive oil-based parenteral nutrition product, IV vitamins and liquid electrolyte replacement due to jejunostomy, case 2 was followed up with enteral nutrition. Polymeric products that prevent weight loss were used. Although Case 3 had STEP surgery, oral intake could not be increased above 2000 kcal/day, and enteral nutrition supplements could not be used due to the possible absence of a salivary gland, lack of teeth, and sleeve gastrectomy. Case 3 is followed up with an olive oil-based parenteral product for 3 days every 3 weeks. In patients with SBS, fat-soluble vitamin deficiencies (A, D, E and K), water-soluble vitamin deficiencies, vitamin B12, zinc, copper, selenium and iron deficiencies should be expected depending on the location and length of bowel resection. Clinical signs and laboratory findings of these deficiencies should be monitored.[6] In Case 1, micronutrient needs were replaced daily. Vitamin D was replaced IM. Three ampoules of vitamin K were replaced IV annually, although the INR was not prolonged (bleeding complications). Multivitamin and multimineral preparations are given once daily in case 2 and twice daily in case 3. However, vitamin D and B12 needed IM supplementation, and iron deficiency was replaced with IV.

In patients with SBS, fluid volume abnormality appears as hypovolemia or hypervolemia. Chronic dehydration, which is frequently encountered, can cause fatigue, nephrolithiasis, acute kidney injury, and chronic kidney disease. Oral and IV fluid intake, urine amount, stoma output amount and, if any, stool amount, urine Na, kidney function tests and weight should be monitored. Oral rehydration fluids can be used during the adaptation period. Hypertonic or hypotonic oral fluid intake should be avoided. Pa-

tients may need additional interventions such as periodic or daily PN or intravenous (IV) fluids, depending on the extent of bowel resection and the presence of a stoma.[6] A target of 1000-1200 ml/day urine output should be frequently recommended. In Case 1, fluid needs were replaced parenterally. There was no hydration problem in Case 2. In Case 3, hypervolemia was frequently encountered due to CHF and CKD. Diuretic treatment was initiated and was adjusted with proBNP monitoring.

In patients with Short Bowel Syndrome and intestinal motility disorder, the location and length of intestinal resection affect drug absorption. In addition, colon microbiota is necessary for vitamin K synthesis. Warfarin is absorbed in the stomach and proximal small intestine. Intestinal motility disorder, changes in colon microbiota, and vitamin K replacement, especially in patients receiving HPN, may pose difficulties in warfarin treatment.[7] This has led to the choice of direct-acting anticoagulant treatment (rivoraxaban). Case 2 is followed with half a warfarin tablet daily. The patient presents with intermittent hematuria and renal colic attacks. Case 3 is followed without complications with apixaban. Bone metabolism changes, and osteoporosis occurs in patients with SBS due to fatty tissue change, decrease in hormones produced from the intestine (GLP1, GLP2, GIP, glucagon, disruption of the intestine-bone axis), vitamin D and K malabsorption, calcium and magnesium malabsorption, kidney and liver damage.[8] In Case 1, osteopenia developed in the 5th year of follow-up and osteoporosis in the 10th year. Vitamin D support was provided. Osteopenia wasn't detected in Case 2. In Case 3, the patient was osteoporotic preoperatively and is receiving vitamin D supplementation.

In patients with SBS, parenteral nutrition complications such as sepsis, fatty liver after blood transfusions, steatohepatitis, liver failure, cholestasis, and gallstones may be encountered.[9] In Case 1, early-period liver enzyme elevation improved when daily vitamin administration was discontinued. In Case 2, elevated liver enzymes were considered to be caused by overfeeding and parenteral nutrition was discontinued. Instead of a multi-chamber bag, the lipid was cut, and amino acid and glucose solutions were administered. Following this, the liver enzymes regressed. Liver enzyme elevation developed when parenteral nutrition calories were given according to the patient's original weight to increase weight after weight loss. During another liver enzyme elevation in Case 1, a cholecystitis-cholangitis attack was considered and was intervened with ERCP. Since the patient's liver enzyme levels remained stable and slight hyperbilirubinemia continued, ursodeoxycholic acid was initiated and was beneficial. Case 2 also developed gallstones but is still being monitored without complications. He is being monitored with moderate elevation of liver enzymes due to liver infarction. Case 3 cholecystectomy was performed before short bowel disease. She is being monitored without liver enzyme elevation. In gastrointestinal complaints, cases 2 and 3 in gastrointestinal complaints benefited from PPI, a pancreatic enzyme, loperamide and ursodeoxycholic acid treatments for dyspepsia, diarrhea and tenesmus. Acute kidney injury, chronic renal failure, calcium oxalate stones and recurrent urinary infections are the nephrological problems encountered, especially in patients with intact colon, especially for the latter two.[6] Diet and fluid-electrolyte balance and prevention of recurrent infections are recommended to prevent the development of kidney damage. Recurrent AKI was encountered in Case 1. In case 2, calcium oxalate crystals and renal colic attacks are observed, and in case 3, CKD is observed. HPN therapy is a vital treatment for some patients with short bowel syndrome. However, catheter-related bloodstream infections are associated with life-threatening complications, especially sepsis, septic shock, and metastatic infections.[10] In Case 1, catheter infection was a frequent and life-threatening problem.

In conclusion, short bowel syndrome requires nutritional therapy and multidisciplinary management of infectious, renal, hepatobiliary and bone metabolism complications caused by disease and nutrition. Advanced age, the presence of an underlying chronic disease and follow-up procedures also affect the patient's clinical morbidity and mortality.

Ethics Committee Approval: The patients have signed an informed consent form, and the study was conducted following international guidelines.

Conflict of Interest: No conflict of interest was declared by the authors.

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