

Case Report

Bleeding tendency in an adolescent with chronic small bowel obstruction

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We report a case of fat-soluble vitamin deficiency in a 14-year old boy who had chronic duodenal obstruction. He presented with periodic unexplained bleeding tendency. The laboratory results showed positive fat globules in stool and prolonged prothrombin time. His further investigation revealed low plasma vitamin A and undetectable plasma vitamin E. After parenteral vitamin K and oral vitamin A and E supplement, these abnormalities resolved although he still had absent knee jerk. We propose that fat malabsorption and fat-soluble vitamin deficiency can occur after prolonged duodenal obstruction that induce bacterial overgrowth following by bile acid deconjugation. Despite very few case reports, screening for fat malabsorption and fat-soluble vitamin deficiency might be warranted in patients with chronic small bowel obstruction.

Key Words: bleeding tendency, fat-soluble vitamin deficiency, vitamin K deficiency, small bowel obstruction, blind loop syndrome

INTRODUCTION

Common causes of fat malabsorption are short bowel syndrome,^{1,2} intestinal resection,³⁻⁵ cholestatic liver disease,⁶⁻⁷ abetalipoproteinemia,⁸ and cystic fibrosis.⁹ All of which can lead to fat-soluble vitamin and essential fatty acid deficiencies.¹⁰ We report a patient with chronic small bowel obstruction which is an uncommon cause of fat malabsorption, presented with bleeding tendency.

CASE REPORT

A 14-year old boy was referred to King Chulalongkorn Memorial Hospital, Bangkok, Thailand, due to intermittent unexplained bleeding tendency for 3 years. One year prior, he had recurrent abdominal pain and distension as well as bilious vomiting. His symptoms were later diagnosed as malrotation resulting in Ladd's procedure. After the surgery was done, he still had recurrent vomiting and abdominal distension which showed some improvement after supportive treatment. He reported no history of loose stool or steatorrhea.

One-year postoperative period, he was repeatedly admitted due to multiple bruises on both legs without history of trauma and a large hematoma at the site of intramuscular injection. There was no history of petechiae, ecchymosis, gingival bleeding or hematuria. These bleeding episodes improved after fresh frozen plasma transfusion. He had no symptom of night blindness or sign of reduced dark field adaptation. He was then referred for further investigation. Physical examination revealed a wasted and stunted boy. His body weight was 25.9 kg (z score < -3), height 140 cm (z score -3.2), body mass index 13.2 kg/m² (z score -3.8). Eye examination showed

normal cornea, no Bitot's spot nor abnormal pigmentation. Abdominal examination revealed soft abdomen with visible bowel loop and increased bowel sound. Neurological examination demonstrated absent deep tendon reflex in lower extremities. Tandem gait and Romberg's sign were negative. He showed no sign of puberty. Other physical examinations were unremarkable. The following were initial laboratory investigations; Hb 8 g/dL, Hct 31%, WBC 6,360/μL, neutrophil 66.2%, lymphocyte 22.4%, platelets counts 415,000/μL, prothrombin time 216.4 sec (normal range 9.6-14.1), INR >10, partial thromboplastin time 196.7 sec (normal range 29-44) and bleeding time 1.3 min. Peripheral blood smear showed hypochromic microcytic red blood cell with anisopoikilocytosis and polychromasia; however, no acanthocyte presented. Hemoglobin typing was compatible with hemoglobin H disease.

Since the platelet count and bleeding time were normal and there was neither family history nor childhood bleeding tendency, this acquired secondary hemostatic disorder was most likely due to vitamin K deficiency. Coagulation factor VIII and factor IX assays were also reconciled. Prolonged prothrombin time significantly improved after parenteral vitamin K administration.

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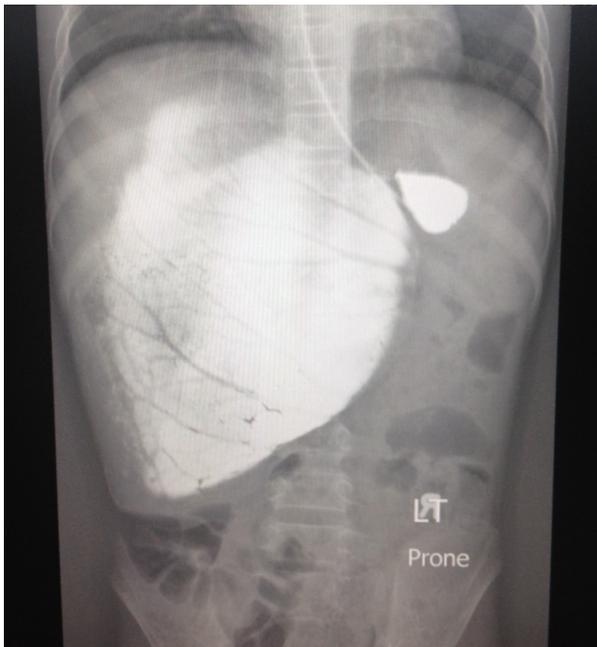


Figure 1. Upper GI study demonstrated duodenal obstruction, likely at post bulbar portion. The barium could not pass into more distal portion of the duodenum.

He underwent further investigations regarding recurrent gut obstruction. The abdominal x-ray showed different air-fluid levels with markedly dilated duodenum with subsequent contrast study showing duodenal obstruction, likely at post bulbar portion (Figure 1). The endoscopic examination demonstrated a stenosis below 2nd part of duodenum with marked proximal dilatation. He then went through exploratory laparotomy with duodenoduodenostomy and duodenal plication. During post-operative period he was put on long-term parenteral nutrition due to feeding intolerance despite various semi-elemental and elemental formulas as well as jejunal feeding. His stool Sudan stain for fat was positive pre- and post-operatively. During this hospital admission, nerve conduction velocity showed chronic asymmetrical sensorimotor, axonal predominate, peripheral neuropathy of

lower extremities which was compatible with vitamin E deficiency.

Due to persistent feeding intolerance, upper endoscopy was performed which demonstrated good patency of the anastomotic site with marked dilatation of 1st and 2nd part of duodenum. The 2nd exploratory laparotomy was done with gastrojejunostomy and duodenal plication. Duodenal biopsy revealed strips of benign intestinal mucosa with prominent Brunner's glands and intact villi. Duodenal fluid culture demonstrated *E.coli* 6×10^6 CFU/mL, *Citrobacter* sp. 5×10^6 CFU/mL, and Viridans Streptococcus 13×10^6 CFU/mL. This finding was compatible with small bowel bacterial overgrowth.

His feeding intolerance was gradually improved in 3 months; therefore, he was discharged home on medium-chain triglyceride (MCT) added diet in addition to lactose-free MCT formula (approximately 600 kcal per day from MCT). He was also given intramuscular vitamin K 6 mg once a month, vitamin E 200 IU three times per day, multivitamin (composition/cap : vitamin A 25 IU, vitamin D-2 300 IU, vitamin B-1 1 mg, vitamin B-2 0.5 mg, niacinamide 7.5 mg, vitamin C 15 mg) three times daily. Fat-soluble vitamin level was shown in Table 1. He also received cyclic oral metronidazole every month.

One year post-gastrojejunostomy, he still had poor weight gain with intermittent steatorrhea and abdominal distension. Further surgical options such as reduction tapering duodenoplasty or pancreaticoduodenectomy were considered to be too risky due to possible pancreatic duct injury and other complications. Consequently, intermittent parenteral nutrition, MCT diet, and fat-soluble vitamin supplement were still needed in this patient. During the course of nutritional rehabilitation, he showed no clinical or laboratory evidence of essential fatty acid deficiency as demonstrated by the triene: tetraene ratio <0.4 .

DISCUSSION

This patient presented with unexplained bleeding tendency. Initially vitamin K deficiency was not recognized as primary cause for several years. Despite several reports

Table 1. Laboratory plasma vitamin levels, coagulograms and lipid profiles

Lab	Before the 2 nd operation [†]	During PN [§] therapy	4 months after the 3 rd operation	1 year after the 3 rd operation
Vitamin A (normal value 20-50 µg/dL)	18.7	79.7	21.9	28.2
Vitamin D (normal value 30-100 ng/mL)	41.1	-	39.8	59.9
Vitamin E (normal value 700-1200 µg/dL)	Not detected	1501.4	290.1 [¶]	1133.8 ^{¶¶}
Prothrombin time (second)	21.1/13.8	-	17.8/12.2	14.1/12.2
INR [‡]	1.62	-	1.45	1.2
Cholesterol (mg/dL)	-	125	48	71
Triglyceride (mg/dL)	-	87	51	41
High density lipoprotein (mg/dL)	-	28	21	31
Low density lipoprotein (mg/dL)	-	79.6	14	30
Vitamin B-12 (pg/mL)	-	792	-	-
Folate (ng/mL)	-	>20	-	-
Triene:tetraene ratio (C 20:3 n-9/C 20:4 n-6)	-	-	0.028	-
Stool for fat	positive	positive	-	positive

[†]4 years after the 1st operation

[‡]INR: International normalized ratio

[§]PN: parenteral nutrition

[¶]on vitamin E 100 IU alternate day

^{¶¶}on vitamin E 200 IU three times per day

Table 2. Previous case reports of fat malabsorption from blind loop syndrome

Author	Age/Sex	Diagnosis	Serum vitamin	Presentation
Stewart et al ¹¹	3 years/female	Necrotizing enterocolitis S/P terminal ileum to distal sigmoid colon resection and ileosigmoidostomy	-	- abdominal pain and distension - vomiting - steatorrhea - hypoalbuminemia
	4 months/male	Gastroschisis and small bowel atresias S/P small bowel resection with Bishop-Koop enterostomy	Low vitamin D	- abdominal distention - vomiting - steatorrhea - hypoalbuminemia - prolonged coagulation times
	11 years/female	Biliary atresia S/P Kasai operation and bilioenteric conduit	Low vitamin A Low vitamin D	- abdominal pain - steatorrhea - hypoalbuminemia
Kilby et al ¹²	3 years/male	Jejunal atresia S/P jejunal resection and end-to-back anastomosis	-	- malnutrition - fat malabsorption
Bayes et al ¹³	10 years/male	Ileal atresia S/P ileal resection and side-to-side anastomosis	-	- malnutrition - fat malabsorption
	40 days/male	Esophageal, duodenal, colonic atresia S/P gastrostomy, end-to-side duodenojejunosomy and Rt. transverse colostomy	-	- malnutrition - fat malabsorption
	2 weeks/female	Jejunal atresia S/P gastrostomy and end-to-side duodenojejunosomy	-	- fat malabsorption
	2 years/female	Jejunal obstruction S/P jejunal resection and end-to-end anastomosis	-	- fat malabsorption
Brin et al ¹⁵	40 years/male	Bleeding ulcer S/P stomach and duodenal resection, proximal stomach and jejunal anastomosis	Vitamin E ($\mu\text{g/mL}$): 0.2 (5-15) Vitamin A (mg/dL): 14 (25-75)	- weakness, ataxia - absent deep tendon reflex - peripheral neuropathy - ophthalmoparesis - pigmentary degeneration of retina
Schjonsby et al ¹⁶	80 years/female	Multiple and large diverticula in duodenum and jejunum	-	- osteomalacia - fat malabsorption
Manicourt et al ¹⁷	37 years/female	Congenital megaduodenum	Vitamin D (25-OH) (ng/mL): 8 (12-24)	- osteomalacia - fat malabsorption

about vitamin K deficiency from fat malabsorption due to different etiologies,⁵⁻⁷ we have found very few case reports of vitamin K deficiency resulting from duodenal obstruction or blind loop syndrome.¹¹ A well-known cause of fat-soluble vitamin deficiency is cholestatic liver diseases. Biliopancreatic diversion or duodenal switch could also cause fat malabsorption leading to the deficiency of fat-soluble vitamin. Slater *et al.*⁵ found the prevalence of vitamin K deficiency to be up to 68% for patients who underwent these types of bariatric surgery.

Another common cause of fat malabsorption and fat-soluble vitamin deficiency is short bowel syndrome. However, our case did not have short bowel syndrome but had fat malabsorption following chronic duodenal obstruction. It was evident from his previous history of chronic abdominal pain and growth failure preceding the Ladd's procedure and bleeding episodes. We summarize previous case reports of fat malabsorption from small bowel obstruction and blind loop syndrome in Table 2.

Those with short bowel syndrome were excluded.

Stewart *et al.*¹¹ reported 3 cases of blind loop syndrome in children. Only one case was demonstrated to have prolonged coagulation time. This 4-month old boy was diagnosed as gastroschisis and intestinal atresias. The atretic bowel was resected and intestinal continuity was restored by a Bishop-Koop enterostomy. He developed abdominal distention, feculent vomiting, steatorrhea, hypoalbuminemia, vitamin D deficiencies and prolonged coagulation times as well as showed evidence of small bowel bacterial overgrowth. The author postulated the bacterial overgrowth and bile acid deconjugation in the stagnant loop resulting in fat malabsorption. Kilby *et al.*¹² reported a case of a 3 year-old boy with jejunal atresia who underwent small bowel resection in neonatal period with end-to-back anastomosis. Six months after the operation, he developed malnutrition, abdominal distension, fat malabsorption so he was diagnosed as stagnant loop syndrome with small bowel bacterial overgrowth. Bayes

*et al.*¹³ demonstrated the blind loop syndrome in 4 children presenting with fat malabsorption and poor growth. Two of them had partial small bowel resection in order to remove the obstruction part which dramatically improved steatorrhea. The other two cases had no anatomical obstruction but did have some stasis; steatorrhea improved after the antibiotics were given. Nevertheless, except for one case reported by Stewart *et al.*,¹¹ all of these 8 children had neither history of bleeding tendency nor abnormal coagulation time. Therefore, we hypothesized that our case of duodenal stenosis with resulting in chronic duodenal obstruction was consistent with the description of 'the blind loop syndrome' which was described as dilated, stagnant segment of intestine which predisposes to bacterial overgrowth of both aerobic and anaerobic species.¹¹ We postulated that bacterial overgrowth in the proximal duodenum could deconjugate bile acids and resulting in fat malabsorption and fat-soluble vitamins deficiencies.¹⁴

There were other case series in adult patients diagnosed as having the blind loop syndrome. Brin *et al.*¹⁵ presented a case of progressive spinocerebellar and retinal disorders following gastric and duodenum resection. In this case, the remaining of the proximal stomach was anastomosed to jejunum and thus blind loop formation. Serum vitamin A level in this case was lower than normal range which then recovered after supplementation.

There were also two reported cases of osteomalacia in adults with fat malabsorption from stagnant loop syndrome. The authors of both reports postulated that there might be an association of small bowel bacterial overgrowth and increase bile acid deconjugation.^{16,17}

To recap, our case report presented with bleeding from vitamin K deficiency and demonstrated the classic clinical findings of vitamin E deficiency. Despite low plasma vitamin A level, we did not find retinal signs of vitamin A deficiency. He also had normal plasma vitamin D level (25-hydroxyvitamin D). It might be explained from adequate sun exposure. We proposed that his fat malabsorption and fat-soluble vitamins deficiencies were due to duodenal obstruction induced bacterial overgrowth and bile acid deconjugation. Certain bacterial species can produce deconjugating and dehydroxylating enzymes resulting in deconjugation of conjugated bile salts in the duodenum. Moreover, the low intestinal lumen pH that resulted from stagnation and excessive fermentation may precipitate free bile acids and favor more nonionic diffusion of the conjugated bile salts. Thus the effective concentration of bile salts fall below those required for micelle formation.¹⁴ Unfortunately, from the severity of his anatomical abnormality and stasis, he did not response well to cyclic oral antibiotics. Apart from the postulation of bile acid deconjugation from small bowel bacterial overgrowth, primary causes of fat malabsorption such as abetalipoproteinemia or chylomicron retention disease were also considered. However, the parents' lipid profiles appear normal and the small bowel biopsy is not compatible with these diagnoses.

Conclusions

Proximal small bowel obstruction is an uncommon cause of fat malabsorption and fat-soluble vitamin deficiency.

Stasis condition or blind loop syndrome can cause bacterial overgrowth resulting in bile acid deconjugation. We presented a rare case of vitamin K deficiency following chronic duodenal obstruction. This patient presented with bleeding tendency and was treated symptomatically for several years without recognition of the underlying cause from secondary vitamin K deficiency. Furthermore, vitamin E deficiency, the most common fat-soluble vitamin deficiency, should always be looked for since clinical presentation may be subtle, as in this case who has never complained of ataxia or weakness despite an undetectable vitamin E level. Therefore, fat-soluble vitamin deficiency and fat malabsorption should be suspected and screened in the case of chronic small bowel obstruction especially those with clinical symptoms such as growth failure, bleeding tendency, and peripheral neuropathy.

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The case report was approved by the Ethics Committee of the Faculty of Medicine, Chulalongkorn University.

AUTHOR DISCLOSURES

None of the authors has any conflict of interest.

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慢性小腸阻塞的青少年其出血傾向

本文報告一位慢性十二指腸阻塞的 14 歲男孩，顯現脂溶性維生素缺乏的病例。病患有周期性不明原因的出血傾向。檢驗結果顯示糞便中有脂肪球及特別長的凝血酶原時間。進一步檢查發現低血漿維生素 A 及偵測不到維生素 E。在靜脈維生素 K 及口服維生素 A 及 E 補充後，這些異常症狀消失，但他仍然缺乏膝反射。可能長時間的十二指腸阻塞進而誘導細菌過度生長以致膽酸早期解離，使得脂肪吸收不良及脂溶性維生素缺乏。儘管此類病例報告很少，患有慢性小腸阻塞的病人，有必要做脂肪吸收不良及脂溶性維生素缺乏的檢測。

關鍵字：出血傾向、脂溶性維生素缺乏、維生素 K 缺乏、小腸阻塞、盲環症候群