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SHORT REPORT

Use of a fish oil-based lipid emulsion to treat essential fatty acid deficiency in a soy allergic patient receiving parenteral nutrition

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Summary The treatment of essential fatty acid deficiency (EFAD) in a 17-year-old male following allogeneic bone marrow transplantation is described. His transplant was complicated by gastrointestinal bleeding that precluded the use of enteral feedings. Due to a severe soy allergy, he could not tolerate any intravenous fat emulsions marketed in the US. After months of receiving fat-free parenteral nutrition and intermittent use of enteral feeds, he developed signs and symptoms consistent with EFAD, including a rash and an elevated plasma triene:tetraene ratio of 0.231 (0.013–0.05). After receiving FDA approval, a parenteral fish oil emulsion was administered to provide fat calories and sufficient α-linolenic and linoleic acid to

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correct his EFAD. Therapy was initiated at 0.2 g/kg/day and advanced to 0.67 g/kg/day, providing approximately 45 mg/kg/day of linoleic acid. After 10 days of therapy, his rash disappeared and his triene:tetraene ratio improved to 0.07. By day 17 the ratio normalized to 0.047. This suggests that using a fish oil emulsion with minimal linoleic acid may be safely used as the sole source of fat calories and may be an option to prevent or treat EFAD in subjects allergic to soy that require a parenteral source of fat.

Introduction

Given that a typical diet contains as much as 30% of energy intake as fat, essential fatty acid deficiency (EFAD) is relatively rare. Patients requiring parenteral nutrition (PN) typically are administered an intravenous fat emulsion (IFE) that consists of soybean oil either alone or in combination with safflower, olive, coconut, or fish oils. EFAD most often occurs in individuals with chronic malnutrition or in those patients receiving prolonged courses of PN with inadequate fat intake.[1] It may occur due to either allergy or hypertriglyceridemia in which IFE cannot be administered and alternative sources of essential fatty acids (EFA) have not been made.[1] EFAD can negatively impact immune system function and impair wound healing.[2,3] In the hospitalized patient, this condition is often overlooked, especially if specialized nutrition support is already being provided.

Case report

In July 2002, the Clinical Nutrition Service at Children's Hospital, Boston was consulted for the treatment of presumed EFAD in a 17-year-old male with gamma-delta T-cell lymphoma who underwent an allogeneic bone marrow transplant. His transplant course was complicated by an early onset of severe acute graft versus host disease (GVHD) with gastrointestinal (GI) bleeding that precluded the use of enteral feedings. His clinical course was further complicated by several food allergies including soy protein, verified by a positive skin test, and peanut protein, that resulted in anaphylaxis prior to this admission. Although he had tolerated products with soy oils in the past, attempts to use parenteral fat emulsions were avoided secondary to concerns with his preexisting soy protein allergy.

Hospital course

The patient was diagnosed in November 2001 with gamma-delta T-cell lymphoma after presenting with abdominal pain. A bone marrow aspiration confirmed this diagnosis. In March 2002, he received an allogeneic bone marrow transplant (5/6 match) from his paternal uncle after a preparative regimen of cyclophosphamide and total body irradiation. He showed signs of early engraftment by day +10 (absolute neutrophil count = 260) concurrent with Grade III acute GVHD of the skin. Significant GI bleeding, and epistaxis starting at day +52, further complicated his transplant course. He subsequently received aggressive transfusion support and desmopressin to improve his platelet function. As his GI bleeding worsened, multiple diagnostic procedures were performed to identify other potential etiologies to his GI bleeding other than GVHD and to identify a possible site for his bleeding. Ultimately, he underwent a push enteroscopy and exploratory laparotomy on day +109 that revealed the presence of submucosal nodules studding the length of the small intestines, consistent with the areas of bleeding. There was no evidence of disease recurrence and only minimal pathological evidence of GVHD in the proximal cecum. The diagnosis of acquired angiodysplasia was made and was treated with conjugated estrogens. His bleeding gradually ceased on this therapy. He developed other therapy-related problems that further complicated his course. Specifically, he developed herpes zoster and *Enterobacter cloacae* sepsis. Stool tests were positive for adenovirus but he did not develop systemic disease. He also developed renal insufficiency, likely related to nephrotoxic medication exposure, hypertension, and hyperglycemia that required insulin therapy. His medical condition continued to deteriorate and on day +115 post-transplant, his family requested that his code and resuscitation status be changed to DNR/DNI (''do not resuscitate/do not intubate'').

Nutritional course

His weight on admission was 59.3 kg (25–50th percentile per NCHS growth charts), his height was 176 cm (50–75th percentile), and his BMI was

19.1 kg/m^2 (10–25th percentile). His ideal weight and BMI were determined to be 65 kg and 21.2 kg/m^2 (50th percentile). His energy requirements were calculated to be 2065–2409 kcal based upon the Schofield equation (basal energy expenditure (BEE) = 1721 kcal with a stress/activity factor of 1.2–1.4). His Recommended Dietary Allowance (RDA) for age was 45 kcal/kg/day, with an estimated protein RDA for age of 0.9 g/kg.

Although oral intake was encouraged between bleeding episodes and the GVHD flair, it was minimal throughout the course of is hospitalization due to nausea and vomiting. As per our practice, PN was started on day 0 of transplantation in order to meet estimated energy and protein requirements.[4] In addition to PN, enteral nutrition (EN) was provided by continuous nasogastric feedings. By day +44, his enteral intake was estimated to be adequate (approximately 1800 kcal/day) and PN was discontinued. To achieve optimal energy intake, a trial of EN with a more concentrated formula (Nutren® 1.5, a soy oil-free enteral formula, 50% MCT (Nestle Nutrition, Glendale CA)) was started despite a high stool output (average 1000 ml/day) on day +52. His weight at the time was 48.4 kg. He failed enteral feedings after 4 days and continued to lose weight (wt = 45.2 kg) despite intravenous fluid management to maintain an adequate state of hydration. PN was resumed and EN was continued although stool output remained as high as 1600 ml/day. On day +50, his PN was again discontinued as his enteral intake increased. Despite reaching a total of 3600 kcal/day and 3 g of protein/kg/day within a week, he failed to gain weight. He was maintained solely on enteral feedings until the recurrence of bloody stools. He underwent an esophagogastroduodenoscopy and colonoscopy on day +60 to evaluate his increased stool frequency and hematochezia. His GI bleeding subsequently worsened and PN support was reinstituted. Enteral feedings were discontinued on day +83. Approximately 10 days after resuming PN without enteral feeding, he exhibited a waxing and waning skin rash. The differential diagnosis at that time included chronic GVHD, EFAD, herpes, and acneiform folliculitis. Given his poor nutritional intake (Table 1) and continued decline, other options for intravenous fat supplementation to provide adequate fat calories and EFA were considered. In light of his past history of soy protein allergy, a plasma EFA profile was obtained to evaluate the need of an IFE infusion. Using capillary-column gas–liquid chromatography to determine fatty acid status, the resulting EFA profile showed an elevated triene:tetraene ratio of 0.231 (range 0.013–0.05), consistent with EFAD (Table 2). Although a pre-transplant skin test was positive for soy allergy, a radioallergosorbent test (RAST) performed post-transplant for soy and egg protein were both negative (RAST to soy $<$0.35 IU/ml, egg $<$0.35 IU/ml, total IGE 40 IU/ml). Because of the risks associated with EFAD and the history of soy protein allergy in this patient, a graded challenge to parenteral soybean oil fat emulsion (Intralipid® 20%, Baxter Healthcare/Fresenius Kabi, Clayton, NC), was performed starting with 1% of the daily dose. After receiving a test dose of 0.2 ml (40 mg) intravenously, he complained of difficulty breathing and developed tachypnea and flushing. His blood pressure and oxygen saturation remained normal. He was treated with a single dose of epinephrine and diphenhydramine with a resolution of his symptoms. Since desensitizing food allergies are unsuccessful,[5] we pursued other alternatives to soy containing parenteral fat emulsions. Although the effect of topical oils on EFA profiles is not predictable, corn oil was applied to his skin while other product alternatives were

Table 1 Macronutrient composition of the infused parenteral nutrition solutions before and after introduction of a fish-oil-based lipid emulsion.

Macronutrient	Immediately prior to diagnosis of EFAD		At time of normalization of triene:tetraene ratio after introduction of Omegaven™	
	Type	Quantity	Type	Quantity
Amino acids	Aminosyn®	69.42 g	Aminosyn®	75.8
Carbohydrate (CHO)	Dextrose	495.25 g	Dextrose	758
Fat		0 g	Omegaven™	27.4
Total (kcal/day)		1961		3181
CHO calories (day)		1683		2577
Lipid calories (day)		0		301
NPC:N_2 ratio		152:1		237:1

CHO: carbohydrate; EFAD: essential fatty acid deficiency; NPC: non-protein calories; N_2: nitrogen.

Table 2 Plasma fatty acid profiles before and after introduction of Omegaven™

Day of therapy		0	4	10	17	24	31	48
Omegaven™ (g fish oil/kg/day)*		0	0.5	0.4	0.6	0.3	0.25	0.25
Measured parameter	Normal range 2–17 years							
Octanoic acid (μmol/l)	9–4	10	9	8	13	10	17	326
Palmitoleic acid (μmol/l)	100–670	3125	3894	2580	2423	2810	2655	1708
A-linolenic acid (μmol/l)	20–120	16	37	78	76	54	49	269
Linoleic acid (μmol/l)	1600–3500	911	750	1271	1101	1028	945	2157
Oleic acid (μmol/l)	350–3500	4551	4941	3741	3244	3894	3294	3568
Vaccenic acid (μmol/l)	320–900	1137	1500	871	456	770	739	792
Stearic acid (μmol/l)	280–1170	860	1182	1700	1698	2060	1554	1702
EPA (μmol/l)	8–90	44	882	2449	2839	2692	1763	1695
Arachidonic acid (μmol/l)	350–1030	790	807	1138	1094	1136	962	779
Mead acid (μmol/l)	7–30	183	163	69	51	32	36	26
DHA (μmol/l)	30–160	62	746	2339	1745	1920	1679	1274
Triene:tetraene ratio	0.013–0.050	0.231	0.202	0.06	0.047	0.029	0.038	0.033
Total saturated (mmol/l)	1.4–4.9	6.4	7.6	8.4	9.2	10.1	8.7	8.3
Total monosaturated (mmol/l)	0.5–4.4	9.6	11.5	7.8	7	8.1	7.4	6.8
Total polyunsaturated (mmol/l)	1.7–5.3	2.4	3.8	8.2	7.9	7.7	6.2	6.9
Total omega-3 (mmol/l)	0.1–0.4	0.2	1.8	5.4	5.4	5.2	4	3.7
Total omega-6 (mmol/l)	1.6–4.7	2.1	1.8	2.7	2.5	2.4	2.1	3.2
Total fatty acids (mmol/l)	4.4–14.3	18.5	23.1	24.5	24.3	26.1	22.3	22.2

EPA: eicosapentaenoic acid; DHA: docosahexaenoic acid.
*Daily dose of Omegaven varied due to fluid restrictions.

Table 3 Comparison of lipid emulsions (10 g fat/100 ml).

Product	Intralipid® (Baxter Healthcare/Fresenius Kabi)	Liposyn II® (Abbott)	Omegaven™ (Fresenius AG)
Oil source			
Soybean (g)	10	5	0
Safflower (g)	0	5	0
Fish (g)	0	0	10
% *Fats*			
Linoleic (g)	50	65	0.1–0.7
α-linolenic (g)	9	4	<0.2
EPA (g)	0	0	1.28–2.82
DHA (g)	0	0	1.44–3.09
Oleic (g)	26	17.7	0.6–1.3
Palmitic (g)	10	8.8	0.25–1
Stearic (g)	3.5	3.4	0.05–0.2

EPA:eicosapentaenoic acid; DHA: docosahexaenoic acid.

investigated. We identified a parenteral lipid emulsion that was soy-free (Omegaven™, Fresenius Kabi AG, Bad Homburg VDH, Germany) (Table 3). As this product is not approved for use in the United States, informed consent, institutional review board, and FDA emergency approvals were obtained prior to its administration.

Omegaven™ treatment was started at a dose of 0.2 g/kg/day (the maximum approved daily dose) IV and advanced to 0.67 g/kg/day, providing approximately 45 mg/kg/day of linoleic acid (LA) (Table 4). After 10 days of therapy, his truncal folliculitis resolved and his overall functional status improved. Also during this time, the plasma triene:tetraene ratio improved to 0.06 (Fig. 1). By day 17 of the Omegaven™ infusion, the triene:tetraene ratio normalized to 0.047. After 30 days on this regimen, the DNR/DNI order was revoked. Enteral feedings were resumed on day +164 (46 days after Omegaven™ had been initiated). PN was discontinued on the day of discharge (day +173). At discharge, his weight had increased to 56.3 kg and his triene:tetraene ratio remained within normal limits (0.033) as did his LA acid levels (2157 μmol/l, range 1500–3500 μmol/l). He received a total of 57 days of PN supplemented with Omegaven™. It served as his sole source of fat calories for 46 days until he could be transitioned to enteral feedings.

Table 4 Summary of maximum fatty acid intake during Omegaven™ therapy.

	7/30 2002	8/5 2002	8/12 2002	8/19 2002	8/26 2002	9/12 2002
Day of therapy	4	10	17	24	31	48
Omegaven™ dose (g fish oil)	22.5	18.24	27.42	14.64	12.28	12.7
Calculated fatty acid intake (maximum)						
Linoleic acid (g)		1.2768	1.919	1.0248	0.8596	0.889
α-linolenic acid (g)	0.45	0.3648	0.5484	0.2928	0.2456	0.254
EPA (g)	6.345	5.14368	7.73244	4.12848	3.46296	3.5814
DHA (g)	6.9525	5.63616	8.47278	4.52376	3.79452	3.9243
Palmitic acid (g)	2.25	1.824	2.742	1.464	1.228	1.27
Palmitoleic acid (g)	2.025	1.6416	2.4678	1.3176	1.1052	1.143
Stearic acid (g)	0.45	0.3648	0.5484	0.2928	0.2456	0.254
Oleic acid (g)	2.925	2.3712	3.5646	1.9032	1.5964	1.651
Arachidonic acid (g)	0.9	0.7296	1.0968	0.5856	0.4912	0.508

EPA:eicosapentaenoic acid; DHA: docosahexaenoic acid.

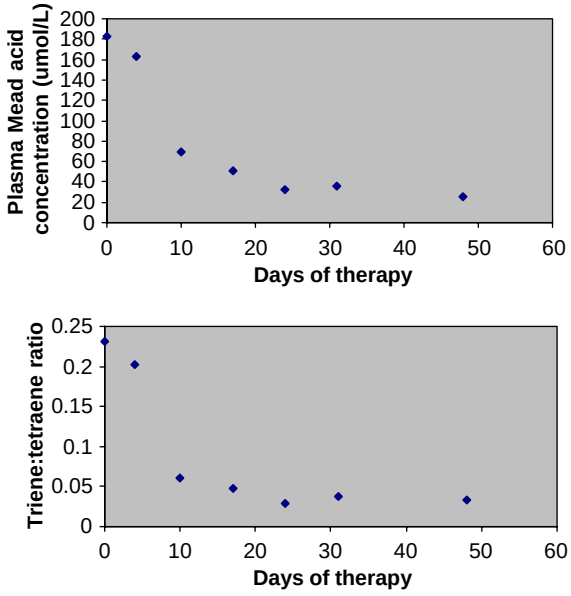

Figure 1 Plasma Mead acid levels and triene:tetraene ratios improve and return to normal after initiation of therapy with Omegaven™

Discussion

In Western countries, the recommended consumption of polyunsaturated fatty acids (PUFAs) is typically equivalent to 7–10% of total energy intake.[2] LA and α-linolenic (ALA) acids cannot be synthesized in animal and human tissues and must be obtained from the diet (plant oils) and are thus considered to be EFA.[2] Other fatty acids can be derived from these two fatty acids. Although the body can derive arachidonic acid (AA) from LA, and eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) from ALA, fish oil is a more efficient source. AA, EPA, and DHA are considered conditional fatty acids because their production may be inadequate in selective conditions. There is an absolute requirement of EFA for growth, reproduction, and health. Young animals deprived of these fatty acids in the diet rapidly display adverse effects such as diminished growth, liver and kidney damage, and dermatitis, which eventually result in death. EFA are precursors of eicosanoids, including prostaglandins (PG_1, PG_2 and PG_3 series), thromboxanes, leukotrienes, and lipoxins. In addition, these fatty acids confer distinctive attributes on the complex lipids that may be required for their function in membranes.[6] Finally, oleic acid is the only PUFA converted via intermediates to Mead acid (5,8,11-eicosatrienoic acid [20:3 omega-9]) that is produced by de novo lipogenesis in animals. As Mead acid typically accumulates in conditions of EFAD, the ratio of this compound to AA [20:3w9/20:4w6], i.e., the triene: tetraene ratio, is used when EFAD is suspected.

Fatty acids are major cellular constituents and form integral parts of the cell membrane that impacts on the membrane's fluidity and function. Within the plasma lipoprotein particles, they serve as the major constituents of phospholipids, triglycerides and cholesterol esters. There are two important classes of long chain fatty acids: omega-3 fatty acids (e.g. ALA, EPA, DHA) and omega-6 fatty acids (e.g. LA, AA). They play a major role in cell structure, providing the integrity of the cell membrane. The membrane composition is determined by the dietary intake of either the omega-3 or omega-6 fats. Depending upon the type of oil ingested, the percentage of EFA will vary dramatically (Table 5). Excess dietary intake of either type of EFA may be associated with adverse effects. Due

Table 5 Percent of fatty acids in oil (% kcal).

Oil	18:2n-6 linoleic	18:3n-3 α-linolenic	20:5n-3 EPA	22:6n-3 DHA
Soybean	54	7	—	—
Safflower	76	0.5	—	—
Sunflower	68	1	—	—
Corn	54	1	—	—
Olive	10	1	—	—
Canola	22	10	—	—
Palm	10	1	—	—
Cottonseed	54	1	—	—
Peanut	32	-	—	—
Linseed	16	54	—	—
Walnut	53	10	—	—
Cod liver	2	2	9	9
Herring	—	—	7	4

EPA:eicosapentaenoic acid; DHA: docosahexaenoic acid. Adapted from: Innis SM. Essential dietary lipids. In: Ziegler EE, Filer LJ, editors. Present knowledge in nutrition, 7th ed. International Life Sciences Institute-Nutrition Foundation: Washington, DC, 1996.

to their pro-inflammatory properties, excessive intake of omega-6 fatty acids results in an unbalanced fatty acyl pattern in cell membrane phospholipids that is associated with increased peroxidative catabolite production.[7,8] Conversely, excessive omega-3 intake may alter cytokine and leukotriene generation.[9] Omega-3 fatty acids compete with LA in the AA pathway, thereby reducing the metabolism of AA to prostaglandin E2 and thromboxane A2, which are both important in mediating inflammation.[8,10] Although the body can synthesize these fats from ALA, this conversion is believed to be inefficient in many people. EPA and DHA are important for the production of nerve tissue, hormones, and cellular membranes. EPA is converted into the series 3 prostaglandins that have anti-inflammatory activity.[11] These fats may help decrease hypertension, reduce elevated cholesterol and triglycerides, prevent atherosclerotic plaque formation, and improve skin conditions such as eczema and psoriasis.[12] Although their mechanism of action has not been completely defined, it has been proposed that they work by inhibiting acyl CoA: 1,2 diacylglycerol acyltransferase, increasing hepatic beta-oxidation, or reducing the hepatic synthesis of triglycerides.[13] Potential toxicities associated with excess intake of omega-3's include an increased bleeding tendency due to prolongation of the bleeding time, a possible decline in renal function due to decreased production of the renal vasodilator prostaglandin E2, and a possible deleterious effect on lipid metabolism.[12,14,15]

EFAD typically occurs when <1–2% of total calories are provided as EFAs in children.[16] In the general population, EFAD is considered to be extremely rare. Due to their limited fat stores, premature infants may develop EFAD in less than a week when EFAs are <4–5% of total calories.[1,17] It may also occur in patients with chronic malnutrition, malabsorption, and in patients receiving prolonged courses of PN without adequate fat calories, as observed in this case report.[1]

Biochemical changes consistent with EFAD can occur in as little as a few days in infants and in several weeks in older children and adults.[1,17] Clinical symptoms of EFAD may appear within 1 week in infants although they may take 4–6 weeks to appear in older patients. Skin lesions are common in patients with EFAD. The skin is typically dry with a scaly rash, often mistaken for acneiform folliculitis. It may exhibit erythema and ooze in the intertiginous areas in infants or may appear as an acrodermatitis enteropathica-like rash in others. As part of the differential diagnosis of the dermatological aspects of EFAD, protein energy malnutrition and both biotin and zinc deficiency should be considered. A fatty acid profile, either from plasma or tissue, is an important diagnostic tool that is often used to confirm the clinical suspicion of EFAD.

Until recently, the diagnosis of EFAD was made by the presence of an elevated triene:tetraene ratio. An upper limit of 0.2 has been suggested to be normal.[18] Levels of >0.4 are considered to be diagnostic of EFAD. With improved methodology, however, more sensitive age-based range criteria have been developed to assess plasma EFA status. Siguel et al have shown that by using capillary-column gas–liquid chromatography to determine fatty acid status, more patients at risk for deficiency could be identified.[19,20] Using these methods, triene:tetraene ratios >0.05 and Mead acid to AA ratios >0.2 have been considered suggestive of EFAD.[20,21] It should be noted, however, that the triene:tetraene ratio does not reflect the omega-3 fatty acid status, as the diets used to evaluate EFAD were deficient in both omega-3 and omega-6 fatty acids.[3] Moreover, this could also suggest that the recommended intakes for LA may actually be higher than actual requirements provided there is adequate intake of omega-3 fatty acids. This may explain why our patient did improve despite receiving a less than optimal intake of LA. This is supported by earlier work by Bourre and colleagues who reported that physiologic symptoms of omega-6 fatty acid deficiency improved at lower LA intakes than at the point when tissue omega-6 levels returned to normal limits.[22] In our experience, prior to Omegaven™

therapy, the triene:tetraene ratio was elevated to 0.231. This ratio improved to 0.06 within 10 days and reached 0.028 after 3 weeks of Omegaven™ treatment.

Significant inverse correlations between percentages of plasma EFA and plasma mono-unsaturated fatty acids were also observed, similar to the observations made by Siguel et al. in the course of developing their baseline ranges for normality of EFA status.[19] They reported that due to de novo lipogenesis, patients with EFAD have decreased plasma LA levels accompanied by major increases in palmitoleic, vaccenic, oleic and Mead acid. This was also the case with our patient. Once therapy with Omegaven™ was started, his biochemical parameters gradually normalized. Within 2 weeks of therapy, both oleic and vaccenic acid levels dropped to within normal limits. Other fatty acids, such as Mead acid, took seven weeks to normalize. Marked increases in Mead acid have been seen in cases of severe LA deficiency. In this patient, prior to starting Omegaven™, his plasma Mead acid level was significantly elevated (183 μmol/l, normal 7–30 μmol/l) and gradually decreased, normalizing to 26 μmol/l by day 48 of therapy (Fig. 1), which was associated with an improvement in his LA status. Initially, his LA level was low (750 μmol/l, normal 1600–3500 μmol/l) but it normalized to 2157 μmol/l by day 48. Other markers of EFAD, such as ALA, normalized within days of starting Omegaven™ (Table 2). His baseline ALA level was only 6 μmol (normal 20–120 μmol/l) but within 4 days of beginning Omegaven™, it increased to 37 μmol/l. By the time his rash disappeared on day 10 of treatment, his ALA level increased to 78 μmol/l. Considering the low content of both ALA as well as LA in Omegaven™, one could postulate that these differences in product composition may have delayed his clinical improvement in comparison to potentially a quicker resolution of symptoms had a conventional (IFE) rich with omega-6 fatty acids had been used.

EFAD may be treated with oral, parenteral, and topical preparations. Dudrick et al.,[23] in their landmark paper describing the use of PN in an infant, used the plasma of the child's parents as a source of EFA since no form of IFE was available. Topical application of safflower and corn oils has been described although results are unpredictable and may take up to three weeks for serum EFA ratios to improve.[24–26] Oral ingestion of safflower or corn oil (5 ml three times a day) has also been used.[24] Enteral fat supplementation was not an option for our patient since his enteral feeds were often held due to recurrent (GI) bleeding. He began topical therapy with corn oil while other parenteral options were being explored. The use of topical therapy several days prior to starting the intravenous Omegaven™ may have contributed to our patient's improved triene:tetraene ratio, although it is unlikely to have been responsible for the dramatic improvement in his biochemical markers and overall clinical state that occurred within a week of beginning the intravenous fish-oil-based lipid emulsion.

Since the 1980s, parenteral fat emulsions in the United States have consisted of either a soybean/safflower or a soybean oil emulsion, both of which are rich in omega-6 fatty acids (Table 3). In addition to the oils, these products contain egg yolk phospholipids, glycerin and water. Typically, these fats are dosed as 2% of the total caloric intake or approximately 2.4 g LA per 2000 kcal to prevent EFAD.[4] Many patients, however, receive up to 40% of their total calories as fat to provide sufficient non-protein calories without increasing carbohydrate intake.

Summary/outcome

To our knowledge, this is the first reported case of using an (IFE) containing primarily omega-3 fatty acids and little LA to treat EFAD. It also describes a method of providing adequate parenteral fat calories in a patient with a soy allergy unable to tolerate conventional (IFEs).

There are currently no soy-free parenteral (IFEs) available in the United States (Table 3). Even structured lipid formulations and olive oil containing fat emulsions have a soy component. At present, there is only one soy-free formulation available. This is a fish oil emulsion that consists primarily of omega-3 fatty acids. Unlike the soy-containing formulations, it is not indicated as a sole source of fat calories, but rather as a supplement for patients receiving PN whose underlying disease may benefit from an increased intake of omega-3 fatty acids.[27] It is thought that appropriate intake of omega-3 fatty acids would improve immunological resistance and offer some protection against inflammatory tissue damage and capillary permeability. Supplementation is contraindicated in patients with impaired lipid metabolism, severe hemorrhagic disorders, or unstable diabetes mellitus.[27] In this case, therapy continued a total of 57 days, significantly longer than the 4 weeks recommended by the manufacturer. No adverse effects were observed despite having several underlying conditions (hypertriglyceridemia, GI bleeding and hyperglycemia) that were listed as

Table 6 Biochemical parameters and liver enzyme activities and before and after introduction of fish-oil based (Omegaven™) lipid emulsion.

Day of therapy		0	4	10	17	24	31	48
Omegaven dose (g/kg/day)		0	0.5	0.4	0.6	0.3	0.25	0.25
Measured parameter	Normal range 2–17 years							
Glucose (mg/dl)	50–115	208	199	143	181	121	145	199
Albumin (g/dL)	3–4.6	2.9	2.9	3.1	3.1	2.6	2.7	2.6
Triglycerides (mg/dl)	<250	383	353	545	666	593	469	389
Blood urea nitrogen (mg/dl)	5–18	135	127	112	94	105	90	90
Creatinine (mg/dl)	0.3–1	2.7	2	2.6	2.6	3	2.9	2.7
Alkaline phosphatase (IU/l)	70–390	153	252	201	218	220	198	273
Aspartate aminotransferase (AST) (IU/l)	2–40	124	201	155	144	108	68	37
Alanine aminotransferase (ALT) (IU/l)	3–30	108	205	240	219	183	131	67
Total bilirubin (mg/dl)	0.3–1.2	7.3	8	7.6	6.5	5.2	4.1	1.4
Direct bilirubin (mg/dl)	0.0–0.4	4.5	5.1	5	4	3.6	2.8	0.7

contraindications. Our patient's GI bleeding was managed with parenteral conjugated estrogens while his hyperglycemia was managed with insulin. Eighteen days after the initiation of Omegaven™, he clinically improved with the disappearance of his acneiform folliculitis, decreased stool output, increased appetite and normalization of the triene:tetraene ratio. For the first time in 5 months he was able to resume normal activities. Prior to his discharge to home, he was transitioned to table foods and enteral supplements. The ability to provide a well balanced PN regimen of carbohydrate, protein, and fat was crucial to his dramatic recovery and, although not intended, our patient may have benefited further from the anti-inflammatory properties of the omega-3 fatty acids in addition to the correction of EFAD as evidenced by his improvement in hepatic enzymes and serum bilirubin levels (Table 6). Additional research in this area is warranted.

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