The oral manifestations of intestinal lymphangiectasia: case report

Patrick M. Ralph, DMD Kenneth C. Troutman, DDS, MPH

Abstract

Intestinal lymphangiectasia is a rare autosomal dominant disorder or acquired condition that leads to lymph obstruction, poor chyle transport, and concomitant problems of hypoproteinemia, lymphocytopenia, hypogammaglobulinemia, and peripheral edema. Patients develop diarrhea, steatorrhea, and hypocalcemia secondary to fat-soluble vitamin malabsorption. Treatment is a restrictive diet of low fat, medium chain triglycerides. Oral manifestations are gingivitis due to poor PMN function and enamel defects due to poor calcium absorption. A case of a 14-year-old boy with both gingival and enamel problems secondary to intestinal lymphangiectasia is reported. (Pediatr Dent 18:461–64, 1996)

Intestinal lymphangiectasia (IL) is a rare disorder of the small intestine characterized by dilated lymphatics. IL has no gender predilection, usually appears in the first decade of life, and may be primary or secondary to lymph obstruction.[1] Primary IL occurs congenitally when lymphatics of the small intestine fail to unite.[2] IL can also be present as an autosomal dominant disorder known as Milroy's disease. As a secondary disorder, lymph obstruction occurs as a result of an inflammatory or neoplastic condition. For example, it can be secondary to messenteric tuberculosis, sarcoidosis, malignant lymphoma, chronic pancreatitis, Noonan's syndrome, and congestive heart failure.[3] IL ultimately interferes with the transport of chyle via the mesenteric, retroperitoneal, or main thoracic lymphatics into the blood circulation, resulting in mucosal dilation.

IL was first described in 1961 by Waldmann et al.[4] As the authors described, patients with IL develop protein-losing enteropathy leading to hypoproteinemia, lymphocytopenia, hypogammaglobulinemia, and peripheral edema. In addition, these patients develop mild to moderate diarrhea, steatorrhea, and hypocalcemia secondary to fat and fat-soluble vitamin malabsorption.

Intestinal lymphangiectasia has been reported sporadically in the literature.[4–13] Bolton et al. reported three patients with primary IL in whom standard in vitro tests of neutrophil function were abnormal.[6] In addition, patients with IL have been shown to have impaired cellular immunity secondary to loss of lymphocytes into the bowel lumen.[14,15] Consequently, these patients potentially have impaired neutrophil (PMN) function. Patients with IL also have compromised calcium and vitamin D homeostasis leading to defects of both hard and soft tissues in the oral cavity.

The most apparent oral complications associated with patients diagnosed with IL are hypoplastic enamel defects (HED) and to a lesser extent, but not insignificant, gingivitis. Both can lead to premature tooth loss. IL patients present a chronic disruptive disorder of enamel enabling one to determine the severity and duration of the morphogenic disturbance from the HED.[16] IL patients have poor calcium and vitamin D homeostasis, resulting in HED, which is often related to the degree of patient compliance with the severely restricted diet. Hypoproteinemia, hypogammaglobulinemia, and hypocalcemia also develop as a result of poor dietary compliance. These deficiencies lead to a decreased quality and quantity of neutrophils and immunoglobulins—the primary immunocytes in the periodontium—and poor gingival status in IL patients.

Management

Successful medical management of IL is related directly to the patient's adherence to the severely restricted dietary therapy. The major goal of management is to eliminate lymphatic obstruction. This is accomplished by placing patients on a low fat, medium chain triglyceride (MCT) diet,[17] which decreases the amount of inflammation in the lumen, thereby allowing proper lymphatic flow to occur. MCTs are unlike long chain triglycerides in that they do not require lymphatic transport. When MCTs are metabolized, they are absorbed directly into the circulation without stimulating lymph flow. This decreases villi dilatation and restores lymphatic flow in order to limit enteric fat, protein, and lymphocyte losses in the bowel lumen.

Case report

Medical history and chief complaint

A 14-year-old white male with complaint of poor dental esthetics was brought to the Columbia-Presbyterian Medical Center (CPMC) pediatric dental clinic.

The patient was a 5 lb, 14 oz product of a full-term uncomplicated pregnancy from a nonconsanguinous marriage. He had no neonatal complications and was discharged with his mother at 3 days of age. From birth to 7 weeks the patient had a history of frequent stools with some respiratory congestion. His physical exam revealed pale skin with periorbital, pedal, and scrotal edema. In addition, the patient had ascites, decreased abdominal girth, left inguinal hernia, and generalized lymphadenopathy. The laboratory evaluation revealed hypocalcemia, hypoalbumenemia, hypoproteinemia, and evidence of fat malabsorption (carotene = 22 mg). Abdominal radiographic review showed distended loops of bowel with increased distance between bowel loops suggestive of bowel wall edema. A bowel biopsy revealed gross dilatation of the lymphatic vessels of the submucosa with normal mucosal architecture. Clinical presentation led to the diagnosis of IL at age 7 weeks. No other family members were affected. By age 14 weeks the patient was maintained on a combination of Progestimil™ and Portagen™ (Mead Johnson Nutritional, Evansville, IN) along with vitamin supplements. At 14 weeks the left inguinal hernia was corrected surgically. From age 14 weeks to the present age of 14 years this young man has been followed at CPMC for extensive problems related to his diagnosis. Due to lack of compliance with the restricted diet, the patient had a history of frequent hospitalizations secondary to episodes of poor calcium and vitamin D homeostasis, hypoproteinemia, hypogammaglobulinemia, and hypoalbuminemia. Due to his fluctuating nutritional status secondary to poor dietary compliance, a short stature and deficient immune system resulted.

Clinical exam

The extraoral examination revealed a pale complexion, dry skin, chapped lips, and periorbital edema (Fig 1). The cervical and submandibular lymph nodes were palpable and slightly tender bilaterally.

Intraoral exam revealed slight adenoid hyperplasia with a midline uvula. The patient had poor oral hygiene and moderate to severe marginal generalized gingivitis. No other soft tissue abnormalities were noted. All permanent teeth were present with the exception of the mandibular right first molar and the maxillary and mandibular third molars. Teeth had hypoplastic enamel defects (Figs 2 and 3)— both the maxillary and the mandibular teeth were equally affected—presenting widespread pitted defects and brown discoloration of the enamel from the occlusal to the cervical third.

Direct bond laminates had been placed on the maxillary permanent central incisors and the right lateral incisor (Fig 4). The mandibular left first permanent molar had been extracted. Caries affected teeth in all quadrants with recurrent decay around all existing restorations. Radiographs confirmed the caries (Fig 5).

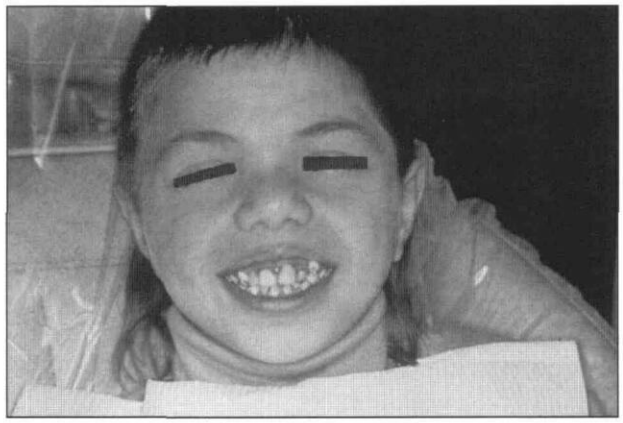

Fig 1. A 14-year-old boy with intestinal lymphangiectasia. Note the periorbital edema and poor esthetics.

Immunologic function tests were not available, however, all serum values were indicative of poor immune function: total protein 3.8 (range = 6.8–8.5), globulin 1.2 (range = 1.5–4.5), albumin 2.6 (range = 3.5–5.5).

Discussion

A thorough review of the literature was conducted to examine the relationship of this patient with other reported cases of IL. Of all cases reviewed, all reported manifestations were related to the gastrointestinal tract, but none to the oral cavity. No significant differences were found between the overall manifestations (e.g., lymphatic obstruction, generalized lymphadenopathy, gross intestinal dilation) of this patient and others reported.

Review of the dental history revealed no familial history of AI or excessive exposure to fluoride, ruling out these causes of enamel defects. The potential for poor oral hygiene as the cause of the gingival problems could not be ruled out, but the possibility of IL contributing to the gingival problem is likely due to its significant systemic effects.

HED and gingivitis are well documented in the literature, however not in association with IL. The excess loss of nutrients into the bowel lumen in patients with IL plays a major role in its pathogenesis. Since the malabsorption of proteins and fat-soluble vitamins can lead to poor immune responses and enamel hypoplasia, it is reasonable to assume that IL contributed to the dental complications seen in this patient. Other hereditary causes had been eliminated.

Persons afflicted with IL have impaired cell-mediated immunity (CMI), which is attributed to the continuous depletion of immunologic proteins into the bowel lumen. In spite of this protein loss, IL patients maintain satisfactory health without an abundance of opportunistic infections. However, they may develop small bacterial infections of the integument, respiratory surfaces, and urinary tract as a result of poor CMI or neutrophil activity.

The defensive role of neutrophils in the oral cavity

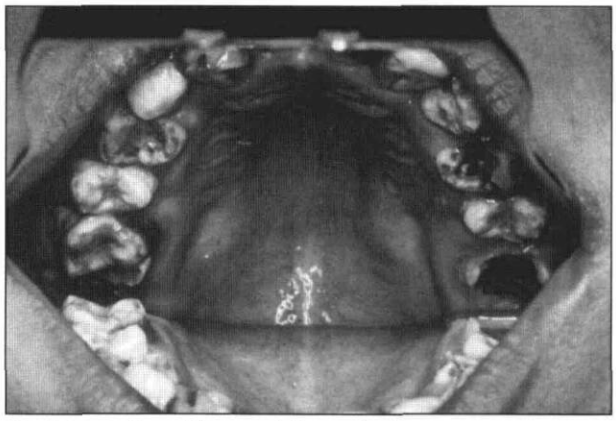

Fig 2. Note the widespread hypoplastic defects of the maxillary arch.

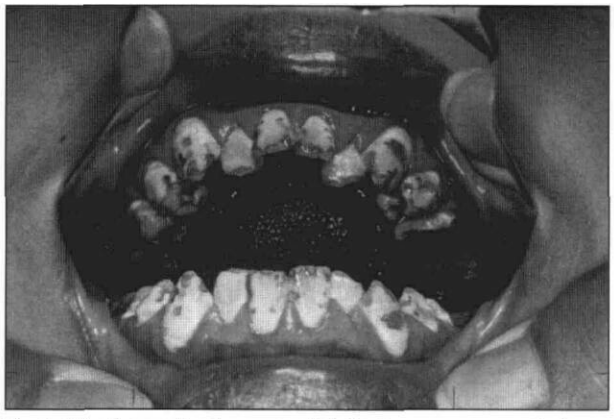

Fig 3. The hypoplastic enamel defects are represented as pitted defects and brown discoloration of the enamel from the occlusal to the cervical third.

is well substantiated by reports that patients with neutrophil function disorders suffer oral infections.[18–20] It has been proposed that an increase in cellular calcium activates various neutrophil functions.[21] Thus, it is possible that hypocalcemia may play a role in decreased neutrophil function, impairing the bacterial defense mechanism of the periodontium in patients with IL. According to Krause et al., the cystolic free calcium concentration in neutrophils is an important determinant of cellular activity.[22] The neutrophil components reflect the involvement of two subcellular structures in intracelluar calcium homeostasis: the calcisome and the plasma membrane.[23] These regulatory components are essential to neutrophil function. If there is a depletion of calcium source—as with IL patients who have poor dietary management—the activation of the neutrophil is affected, potentially leading to poor neutrophil function in the oral cavity.

Bolton et al.[6] suggest that fibronectin, a large molecular weight protein, may play a part in neutrophil chemotaxis.[6] The origin of fibronectin is uncertain, but as a globulin, a lymphocyte origin has been suggested. It has been identified as a receptor on the neutrophil membrane involved in the chemotactic process. A decrease in fibronectin may be expected as a part of the lymphocyte and immunoglobulin depletion, causing an alteration in chemotaxis.[6] This cellular component appears to be essential to the primary function of neutrophils, chemotaxis. With a decrease in fibronectin, the modulatory effects of neutrophils on oral bacteria have been altered, creating an avenue with potential for periodontal destruction for patients with IL.

The homeostasis of calcium and vitamin D plays an important role in the development of the enamel organ. Adults obtain vitamin D through exposure to sunlight. Contrarily, in children absorption of vitamin D is primarily via passive diffusion in the small intestine. Once absorbed in the small intestine, vitamin D is metabolized by the liver and activated by the kidney into 1,25-dihydroxycholecalciferol.[24] This active form regulates the absorption of calcium by acting directly on the enterocyte. If there is a malabsorption of vitamin D there is concomitant decrease in calcium absorption leading to hypocalcemia, and poor mineralization of the enamel organ can ensue. IL patients, when noncompliant with the diet, develop poor vitamin D and calcium homeostasis resulting in hypoplastic enamel defects. Through examination of the patient and the medical history, an obvious disturbance in his vitamin D and calcium homeostasis was noted. Due to poor dietary management, a severe disturbance of the secretory phase of amelogenesis occurred, leading to a clinical manifestation of HED.

In summary, the systemic complications of intestinal lymphangiectasia are directly related to the malabsorption of nutrients secondary to lymph obstruction. The complications have been shown to be controlled by a highly restrictive diet. Lack of compliance with the severely restricted diet is the primary cause of the malabsorption, bringing about intestinal dilation. The development of hypoplastic enamel defects and subsequent gingivitis can potentially diminish in patients who comply with the dietary management. Therefore, management should include consultation with a pediatric dentist.

Dr. Ralph is director, pediatric dentistry component, Bronx Lebanon Hospital and is employed at Segundo Ruiz Belvis Diagnostic and Treatment Center, Bronx, New York. Dr. Troutman is professor of clinical dentistry, Columbia Presbyterian Medical Center, New York, New York.

1. Rudoph, Abraham M: The gastrointestinal tract. In: Pediatrics, 19th Ed. Rudoph AM, Ed. Englewood Cliffs, NJ: Prentice Hall, 1991, pp 1010–11.
2. Moss SF, Thomas DM, Mulnier C, McGill IG, Hodgson HJ: Intestinal lymphangiectasia associated with angiofollicular lymph node hyperplasia (Castleman's disease). Gut 33:135-37, 1992.
3. Gerdes JS, Katz AJ: Neuroblastoma appearing as protein losing enteropathy. Am J Dis Child 136:1024–25, 1982.
4. Waldmann TA, Steinfeld JL, Dutcher TF, Davidson JD, Gordon Jr RS: The role of gastroenterological systems in idiopathic hypoproteinemia. Gastroenterology 41:197–207, 1961.
5. Bawle EV, Black V: Nonimmune hydrops fetalis in Noonan's syndrome. Am J Dis Child 140:758–60, 1986.

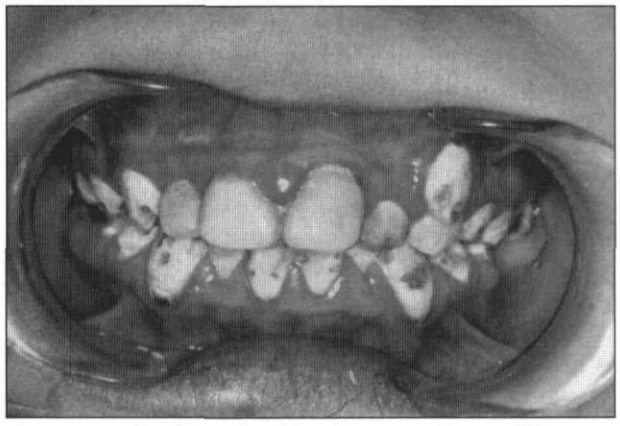

Fig 4. Note the direct bond laminates on the maxillary permanent central incisors and the maxillary right permanent lateral incisor.

6. Bolton RP, Cotter KL, Losowsky MS: Impaired neutrophil function in intestinal lymphangiectasia. J Clin Pathol 39:876–80, 1986.
7. Edees S, Moulden A, Winter RJ: Positive end expiratory pressure via a portable system in thoracic dystrophy. Arch Dis Child 67:136–37, 1992.
8. Nayer HM, Abutalib H, Hugosson C, Al-Mahr M, Ali A: Intestinal lymphangiectasia masquerading as coeliac disease. Annals of Tropical Pediatrics 11:349–55, 1991.
9. Orbeck H, Larsen TE, Hovig T: Transient intestinal lymphangiectasia. Acta Pediatr Scand 67:677–82, 1978.
10. Perisic V, Kokai G: Coeliac disease and lymphangiectasia. Arch Dis Child 67:134–36, 1992.
11. Tift WL, Lloyd JK: Intestinal lymphangiectasia long term results with MCT diet. Arch Dis Child 50:269–76, 1975.
12. Vardy PA, Lebenthal E, Shwachman H: Intestinal lymphangiectasia: a reappraisal. Pediatrics 55:842–51, 1975.
13. Quak SH, Wee A, Yap HK, Tay JSH, Quah TC, Yip WCL: Intestinal lymphangiectasia- a report in two Chinese children. Aust Paediatr J 20:151–53, 1984.
14. Strober W, Wochner RD, Carbone PP, Waldmann TA: Intestinal lymmphangiectasia: a protein-losing enteropathy with hypogammaglobulinemia, lymphocytopenia, and impaired homograft rejection. J Clin Invest 46:1643–56, 1967.
15. Weid PL, Blaese RM, Strober W, Block JB, Waldmann TA: Impaired lymphocyte transformation in intestinal lymphangiectasia: evidence for at least two functionally distinct lymphocyte populations in man. J Clin Invest 51:1319–25, 1972.
16. Suckling GW, Thurley DC, Nelson DGA: The macroscopic and scanning electron-microscope appearance and microhardness of the enamel, and the related histological changes in the enamel organ of erupting sheep incisors resulting from a prolonged low daily dose of fluoride. Arch Oral Biol 33:361–73, 1988.
17. Tift WL, Lloyd JK: Intestinal lymphangiectasia. Long-term results with MCT diet. Archives of Disease in Childhood 50:269–76, 1975.

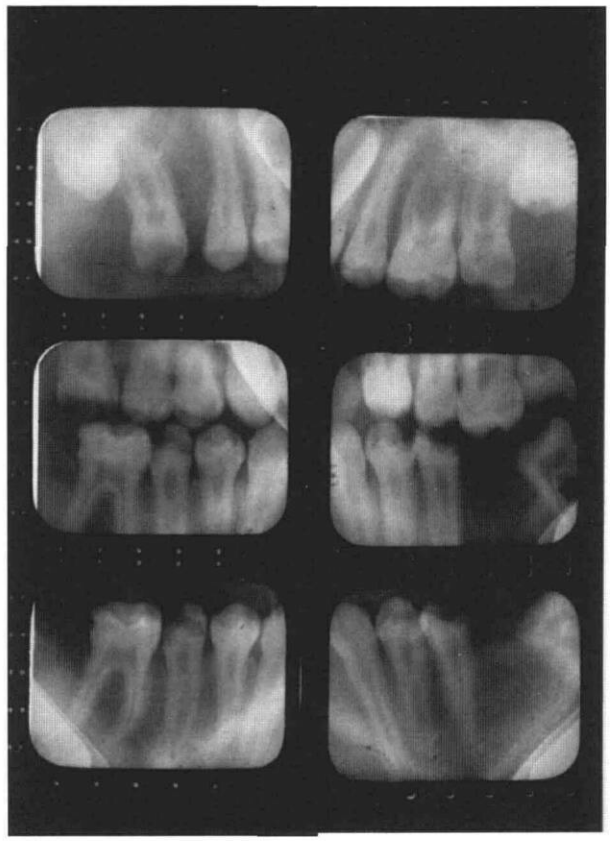

Fig 5. Note the hypoplastic enamel defects on the full-mouth radiograph.

18. Miller DR, Lamster IB, Chasens AI: Role of the polymorphonuclear leukocyte in periodontal health and disease. J Clin Periodontal 11:1–15, 1984.
19. Seow WK: The role of neutrophils in the immunopathogenesis of dental disease. Brisbane: University of Queensland, PhD thesis: 1–395, 1988.
20. Tsai CC, Hammond BF, Baehni P, McArthur WP, Taichman NS: Interaction of inflammation cells and oral microorganisms.VI. Exocytosis of PMN lysosomes in response to gram-negative plaque bacteria. J Periodont Res 13:504–12, 1978.
21. Seow WK, Whitman LM, Bird PS, Thong YH: Modulation of human neutrophil adherence by oral bacteria. Aust Dent J 37:121–5, 1992.
22. Krause KH, Campbell KP, Welsh MJ, Lew DP: The calcium signal and neutrophil activation. Clin Biochem 23:159–66, 1990.
23. Lew DP: Receptors and intracellular signaling in human neutrophils. Am Rev Respir Dis 141:S127–31, 1990.
24. Wapnir RA, Fisher SE: Intestinal secretion and absorption. In: Textbook of Pediatric Gastroenterology, 2nd Ed. Silverberg M, Daum F, Eds. Year Book Medical Publishers Inc, 1988, pp 40–66.