Primary Intestinal Lymphangiectasia Manifested as Unusual Edemas and Effusions

A Case Report

Xuefeng Wang, MD, Hong Jin, MD, PhD, and Weilu Wu, MD

Abstract: Primary intestinal lymphangiectasia (PIL) is a rare disorder of unknown etiology characterized by diffuse or localized dilation and eventual rupture of the enteric lymphatic vessels in mucosa, submucosa, and/or subserosa. Lymph, rich in all kinds of proteins and lymphocytes, leaks into the gastrointestinal tract via the affected lymphatic vessels causing hypoproteinemia and lymphopenia. The main symptom is variable degrees of pitting edemas of bilateral lower limbs. But edemas of any other parts of body, and mild serous effusions may also occur sometimes. PIL occurs in conjunction with a right hemifacial edema, a right upper limb lymphedema, asymmetric bilateral calves edemas, and a unilateral massive pleural effusion seems never to be reported before. In addition, increased enteric protein loss that may cause severe hypoproteinemia usually get overlooked, and the lymphatic system disorders always put the diagnoses in a dilemma.

We described a case of a 17-year-old Chinese girl with a history of gradually progressive swellings of right-sided face, right upper limb, and bilateral calves since 3 to 4 months of age. A right-sided massive pleural effusion, a moderate pericardial effusion, and a mild asciates have been proved unchanged by a series of computerized tomography (CT) scans since 5 years ago. The diagnosis of PIL was finally confirmed by severe hypoproteinemia, endoscopic changes, and histology of jejunum biopsy. Further lymphoscintigraphy and lymphangiography also identified lymph leakage in her bowel and several abnormal lymphatic vessels. A high-protein, low-fat diet supplemented with medium-chain triglycerides (MCT) showed some benefit.

This case suggested that PIL was a rare but important etiology of hypoproteinemia, effusions, and edemas. PIL, effusions, and lymphedema can be the features of multisegmental generalized lymphatic dysplasia. In addition, both lymphoscintigraphy and intranodal lymphangiography could be considered when lymphatic system disorders are suspected.

INTRODUCTION

Primary intestinal lymphangiectasia (PIL) is a rare disorder of unknown etiology characterized by diffuse or localized dilation and eventual rupture of the enteric lymphatic vessels in mucosa, submucosa, and/or subserosa. Lymph, rich in all kinds of proteins and lymphocytes, leaks into the gastrointestinal tract via the affected lymphatic vessels causing hypoproteinemia and lymphopenia. The main symptom is variable degrees of pitting edemas of bilateral lower limbs. But edemas of any other parts of body, and mild serous effusions may also occur sometimes. PIL occurs in conjunction with a right hemifacial edema, a right upper limb lymphedema, asymmetric bilateral calves edemas, and a unilateral massive pleural effusion seems never to be reported before. In addition, increased enteric protein loss that may cause severe hypoproteinemia usually get overlooked, and the lymphatic system disorders always put the diagnoses in a dilemma.

CASE REPORT

A 17-year-old Chinese girl, the daughter of nonconsanguineous healthy parents, presented with a history of gradually progressive swellings of right-sided face, right upper limb, and bilateral calves since 3 to 4 months of age. Edemas firstly occurred on the right-sided face and then expanded to the right upper limb, finally the bilateral calves. She also displayed a discontinuous diarrhea and nausea. A right-sided massive pleural effusion, a moderate pericardial effusion, several hepatic nodules, a mild asciates and many enlarged mesenteric lymph nodes have been proved unchanged by a series of computerized tomography (CT) scans since 5 years ago (Figure 1A). But she denied having cough, dyspnea, fever, chest pain, night sweats or history of tuberculosis (TB), filarial, and surgery. On physical examination, the right hemifacial edema was mild, and the bilateral calves edemas were mild, pitting but asymmetric (the left one was severer than the right one), while the right upper limb edema was severe and woody with a positive Stemmer sign (Figure 1B). A decreased lung sound on the right-sided chest wall was heard. The remainder was unremarkable.

Laboratory tests including stool and urine routine examination, liver, renal and thyroid function, coagulation and blood lipid profiles, electrolytes and assays for human immunodeficiency virus (HIV), hepatitis virus B and C were all unremarkable. Autoantibodies such as antinuclear antibodies, antidouble strand DNA antibodies, antiribonucleoprotein antibodies, anti-Sm antibodies, anti-SSA antibodies, anti-SSB antibodies, anti-SCI-70 antibodies, anti-Jo-1 antibodies, antineutrophil...
cytoplasmic antibodies, antimitochondrial antibodies type M2, antiliver–kidney microsomal antibodies, antiliver cytosol antibodies type 1, and antisoluble liver antigen antibodies were all negative. No filaria was found in her midnight blood. Fecal occult blood test was positive. Her complete blood count revealed a markedly low total lymphocyte count (560 cells/μL) with a reference range 1100–3200 cells/μL, and the percent distributions of CD3+ T cells and CD4+ T cells were 53% and 22.2%, respectively (reference range is 66.9–83.1% and 33.19–47.85% respectively). Total serum protein was 4.00 g/dL (reference range is 6.50–8.50 g/dL), albumin 2.12 g/dL (reference range is 4.00–5.50 g/dL), globulin 1.88 g/dL (reference range is 2.00–4.00 g/dL), but alpha-1-antitrypsin was within the reference range. Thoracentesis demonstrated a straw yellow transudate effusion with negative culture, cytology findings, and tubercular DNA-PCR. Paracentesis of one hepatic nodule showed a hydropic and a fat degeneration of liver cells with many lymphatic cells and Kupffer cells mingling with them. Ultrasonography of 4 limbs’ vessels and heart, gastroscopy, and colonoscopy were all unremarkable. Then a capsule endoscopy was performed and the scattered swollen villi covering on the whole small intestinal mucosa were discovered (Figure 2). Histology of jejunum revealed a series of enlarged lymphatics in mucosa and submucosa (Figure 3) and confirmed the diagnosis of PIL. Further lymphoscintigraphy detected some leakage of radioactivity in her bowel and a poor uptake of 99mTc-human serum albumin in axillary lymph nodes. Intranodal lymphangiography also identified an extremely enlarged left lumbar trunk.

A lifelong, high-protein, low-fat diet supplemented with medium-chain triglycerides (MCT) was prescribed and a tight-fitting stocking was used to control her right upper limb edema. One month later, her total serum protein increased to 5.21 g/dL and albumin 2.97 g/dL. The edemas of lower limbs and right-sided face gradually subsided and the amount of effusions decreased in some degree, while her woody edema remained unchanged.

**DISCUSSION**

The age of onset of edemas suggests a congenital disorder. The asymmetric edemas (especially the right upper limb lymphedema), unilateral massive pleural effusion, and the severe hypoproteinemia are the most important clinical clues. But the cause of hypoproteinemia is the key to appropriate diagnosis. When the likelihoods of malnutrition, impaired protein synthesis (eg, hepatic dysfunction), chronic wasting diseases

---

**FIGURE 1.** (A) The pericardial and pleural effusions. (B) The dramatically swollen right upper limb.

---

**FIGURE 2.** Capsule endoscopic findings: the scattered white dots are in fact the swollen villi that make the appearance of cobblestone road.
Primary Intestinal Lymphangiectasia

Copyright © 2016 Wolters Kluwer Health, Inc. All rights reserved.

FIGURE 3. Hematoxylin–eosin staining of the jejunum: some extremely enlarged lacteal vessels in mucosa and lymphatic vessels in submucosa (magnification ×100).

The authors thank the patient for permitting us to report this case.

ACKNOWLEDGMENT

REFERENCES

1. Braamskamp MJ, Dolman KM, Tabbers MM. Protein-losing enteropathy in children. Eur J Pediatr. 2010;69:1179–1185.

Copyright © 2016 Wolters Kluwer Health, Inc. All rights reserved.

Medicine • Volume 95, Number 10, March 2016
2. Ingle SB, Hinge Ingle CR. Primary intestinal lymphangiectasia: minireview. *World J Clin Cases*. 2014;16:528–533.

3. Vignes S, Bellanger J. Primary intestinal lymphangiectasia (Waldmann’s disease). *Orphanet J Rare Dis*. 2008;3:5.

4. Valdés L, Huggins JT, Gude F, et al. Characteristics of patients with yellow nail syndrome and pleural effusion. *Respirology*. 2014;19:985–992.

5. Fabien M, Jay H. Yellow nail syndrome. *Curr Opin Pulm Med*. 2009;15:371–375.

6. Hennekam RC, Geerdink RA, Hamel BC, et al. Autosomal recessive intestinal lymphangiectasia and lymphedema, with facial anomalies and mental retardation. *Am J Med Genet*. 1989;34:593–600.

7. Connell F, Brice G, Jeffery S, et al. A new classification system for primary lymphatic dysplasias based on phenotype. *Clin Genet*. 2010;77:438–452.

8. Connell FC, Gordon K, Brice G, et al. The classification and diagnostic algorithm for primary lymphatic dysplasia: an update from 2010 to include molecular findings. *Clin Genet*. 2013;84:303–314.

9. Kitsiou-Tzeli S, Vrettou C, Leze M, et al. Milroy’s primary congenital lymphedema in a male infant and review of the literature. *In Vivo*. 2010;24:309–314.

10. Connell FC, Ostergaard P, Carver C, et al. Analysis of the coding regions of VEGFR3 and VEGFC in Milroy disease and other primary lymphoedema. *Hum Genet*. 2009;124:625–631.

11. Hokari R, Kitagawa N, Watanabe C, et al. Changes in regulatory molecules for lymphangiogenesis in intestinal lymphangiectasia with enteric protein loss. *J Gastroenterol Hepatol*. 2008;23:e88–e95.

12. Edward W, Ji H. Lymphangiography to treat postoperative lymphatic leakage: a technical review. *Korean J Radiol*. 2014;15:724–732.