

IMMUNODEFICIENCY DUE TO CHYLOUS DYSPLASIA: DIAGNOSTIC AND THERAPEUTIC CONSIDERATIONS

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ABSTRACT

Among primary immunodeficiencies, common variable immunodeficiency (CVID) is defined by an impaired production of immunoglobulins characterized by low levels of plasma immunoglobulins and an altered antibody response. The case reported here was initially interpreted as a CVID. A 20 year old male suffered from diarrhea, weight loss, and malnutrition. Accurate diagnostic assessment uncovered a protein-losing enteropathy. Conventional oil contrast lymphangiography accurately documented the underlying problem and established the appropriate therapeutic approach. The operation consisted of multiple antigravitational ligatures of dilated and incompetent chylous vessels and chylous vessel-mesenteric vein microanastomoses. Serum albumin and leukocyte counts normalized by 1 week after operation and remained stable with time. There were no more episodes of diarrhea, and the patient regained weight. Accurate diagnostic assessment and particularly lymphangiography may be necessary to properly define difficult cases of immunodeficiency due to intestinal protein loss and to plan a corrective therapeutic functional approach.

Keywords: chylous dysplasia, protein losing enteropathy, immunodeficiency, microsurgery, derivative chylous-venous shunts, lymphography

Among primary immunodeficiencies, common variable immunodeficiency (CVID) is defined by an impaired production of immunoglobulins resulting in low levels of plasma immunoglobulins and an altered antibody response. This case report was initially interpreted as a CVID, but clear information from the patient's medical history and accurate clinical examination pointed to the correct diagnosis and proper treatment.

In chylous disorders, from the immunological point of view, it is important to stem the leakage and loss of immunoglobulins and lymphocytes in order to maintain immunologic competence. Lymph in the thoracic duct contains from about 2,000 to 20,000 lymphocytes per mm³ (a concentration of lymphocytes 2-10 times higher than in the blood). This high lymphocyte count varies according to the number of lymph nodes, temperature, digestive phase, and endocrine status. It is therefore clearly important to restore normal drainage of the intestinal

lymph circulation. In the majority of cases, malnutrition is present with significant hypoproteinemia – specially affecting the albumin fraction – and weight loss. Respiratory problems and steatorrhea are also often present in protein-losing enteropathy (PLE) associated forms (1-5).

In chylous dysplasias, operations should not be undertaken prematurely and need accurate delineation of the nature and site of the likely chylous leak. During this period, the patient should be properly metabolically compensated through an appropriate diet with protein integration and limited lipid input confined only to medium chain triglycerides (MCT). MCTs are preferentially absorbed through the portal venous pathway rather than the intestinal chyliferous route. The addition of water-soluble vitamins (ADEKs tablet) should also be considered.

From the etiopathological point of view, a malformation affecting the thoracic duct, cisterna chyli, and/or chyliferous vessels can cause a significant obstacle to lymph drainage and, in particular, to intestinal drainage. As a result, chyliferous vessels along the walls of the small intestine and of the mesentery become significantly dilated and abnormally stretched due to chylous stasis. The disease also features lymphatic megacollectors with more or less extensive chylous lymphangiectasia, often associated with lymphangiomyomatosis (6-9). In some cases, the chyliferous vessel at the center of the villus breaks into the intestinal lumen, thereby causing the loss of proteins, lipids, lipoproteins, and even calcium and glucose, which leads to metabolic disorders that are typical of so-called PLE.

In this article, we describe a case of immunodeficiency which was due to a PLE. The chylous reflux into the intestinal lumen caused the loss of albumin, antibodies, and lymphocytes to a degree that the patient presented a serious, life-threatening immunodeficiency.

CLINICAL CASE

A 20 year old male suffered from diarrhea (2-4 times a day), weight loss (8 kilos in 5 years), malnutrition (BMI 16.6), hypogammaglobulinemia, hypoalbuminemia, leukocytopenia and lymphocytopenia. After initial interpretation of clinical features as CVID, an accurate diagnostic assessment pinpointed the diagnosis of a PLE. High-resolution ultrasonography demonstrated intrabdominal free fluid, markedly dilated (43 mm diameter) ileal intestinal loops full of intraluminal liquid, thickened highly vascularized intestinal wall (4.5 mm diameter). The test of intestinal protein loss with ^{99m}Tc labeled albumin demonstrated intestinal protein dispersion probably at the ileal region. Lymphoscintigraphy was not clearly indicative of the nature and site of the chylous leakage, however, conventional oil contrast lymphangiography accurately demonstrated the sites of leakage. Lymphography showed markedly dilated lymphatic pathways at the iliac-lumbar-aortic region, mainly on the right side, with dysplastic vessels and gravitational reflux (*Fig. 1*). Cisterna chyli and thoracic duct were normal.

At first, total parenteral nutrition and protein replacement were carried out for about a week without improvement in metabolic alterations. Hypoalbuminemia and lymphocytopenia persisted. Therefore, it was decided to undertake a surgical approach. Dilated chylous vessels were visualized after a fatty meal (60 gm of butter eaten at 4 o'clock in the morning before operation). Operation consisted of multiple antigravitational ligatures of the dilated and incompetent chylous vessels and chylous vessel-mesenteric vein microanastomoses (*Figs. 2,3*). Chylous dysplastic vessels were ligated with non-absorbable suture material. Care was taken not to break these vessels so as to avoid chyloperitoneum. The iliac and right colic regions were the main areas for use of antigravitational ligatures. At the mesocolic area near the right segment of the transversus, two dilated chylous collectors were identified and incised. Both cut-ends

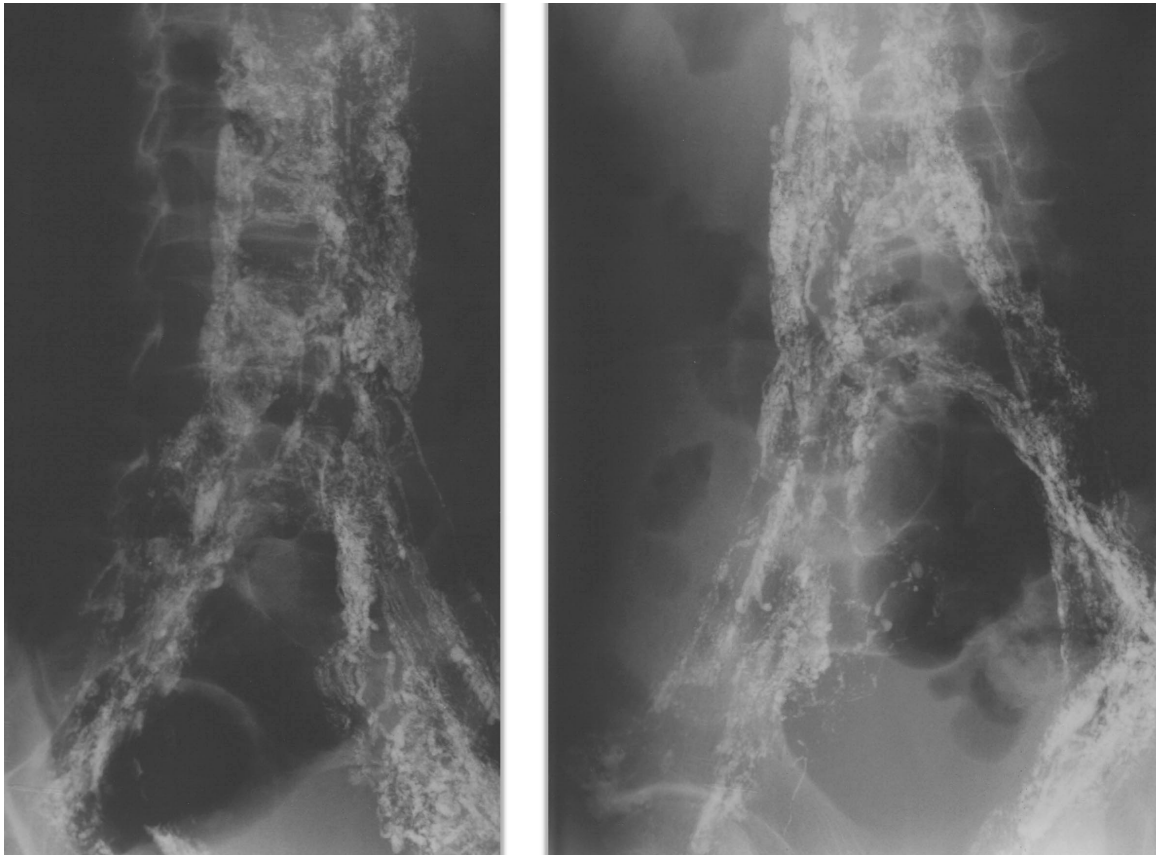


Fig. 1. Lymphogram (posterior on left, anterior view on right) showing dilated lymphatic pathways at the ilio-lumbar-aortic region, mainly on the right side, with dysplastic vessels and gravitational reflux.

were anastomosed to an adjacent mesocolic vein by an end-to-end telescopic technique, using a U-shaped stitch to pull the collectors inside the vein. Other stitches were applied to fix the vessels to the venous stump.

RESULTS

Within a week, metabolic parameters improved and soon reached almost normality. Serum albumin/total protein rose to 3.8/6.4 g/dL, lymphocyte count to 20.2%, and weight to 72 Kg (BMI 21.3) from pre-operative levels of 2.0/3.3 g/dL, 10.1%, and 61 Kg (BMI 16.3), respectively. Post-operative course was favorable and drains were removed after 5 days without reappearance of chyloperi-

toneum. After a week of total parenteral nutrition, the patient started eating a diet regimen with medium chain triglycerides. Presently, at over 5 years from operation, the metabolic condition is stable, there are no signs of malnutrition and the patient is conducting a normal life including gaining weight. Because the chylous dysplasia was very extensive, he is still following an appropriate proper dietary regimen. Thus, the combination of the surgical approach and diet has allowed him to reach a stable condition of metabolic control and normal intestinal function without diarrhea.

DISCUSSION AND CONCLUSIONS

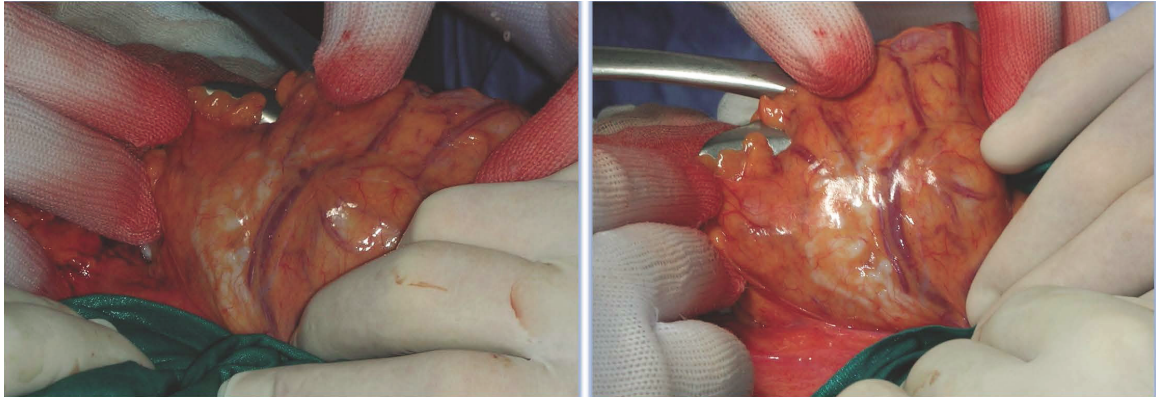


Fig. 2. Chylous vessels are prominent after a fatty meal. They appear dilated and full of chyle.

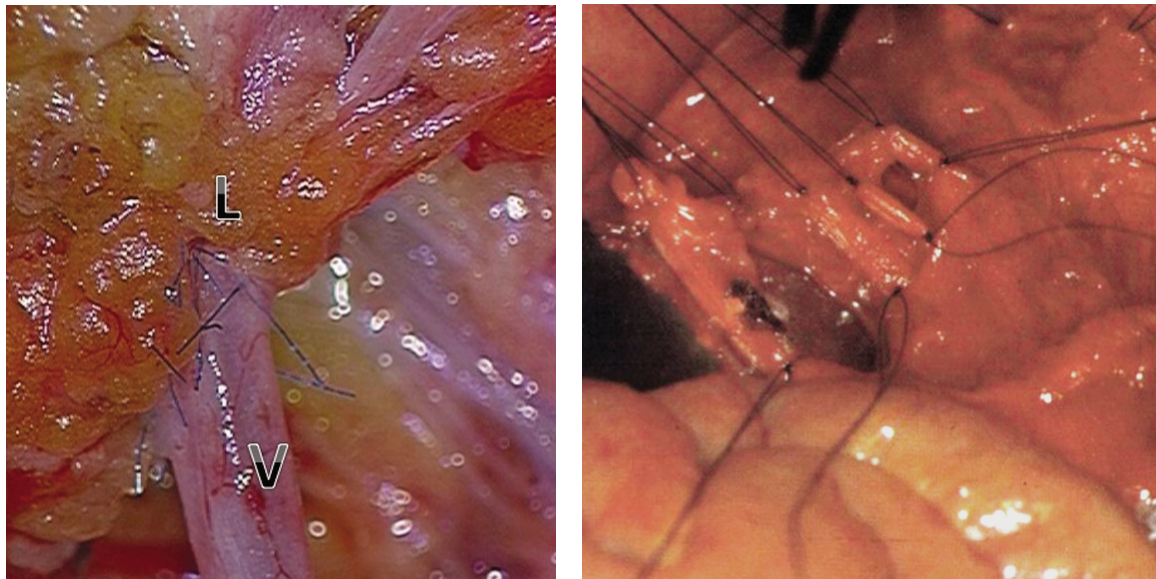


Fig. 3. Lymphatic (L)-mesenteric vein (V) anastomosis (left) and antigravitational ligatures (right).

In this case, the intestinal loss of chyle containing proteins and lymphocytes could not be controlled mandating the surgical approach to reduce this leak. The alternative of a right colectomy could have been considered, but this would have been a symptomatic solution rather than one focused on the causative mechanism. In addition, formation of other areas of gravitational reflux would have been likely because the dysplasia was so extensive. Instead,

performing lymphatic ligatures and diverting the chyle into the blood stream reduced the chylous hypertension producing a favorable and stable result.

The wide ranging extension of the chylous malformations and the complexity of their association with dysplasia of chylolymphatic vessels, thoracic duct, and cisterna chyli explain why, especially in the newborn, sometimes these conditions affect multiple areas and are incompatible with life. Further,

upon clinical onset in the most severe cases, effective treatment may be difficult to achieve later in life, thus leading to more or less complex prognostic implications involving 'quoad valetudinem' (quality of life) as well as 'quoad vitam' (survival) issues (10,11).

In conclusion, considering the etiopathogenesis as well as the nature and complexity of chylous dysplasias, the treatment of these difficult conditions and the outcome significantly depend on the skills of the physicians/surgeons and on the available technology and equipment. For this reason, it is highly recommended that these patients be referred to the few centers that have specific surgical experience in the management of this disease.

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