A Case of Systemic Amyloidosis Found by Goiter in Crohn’s Disease

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Secondary amyloidosis is characterized by accumulation of insoluble, fibrous amyloid proteins in various tissues and organs, accompanied by infectious or inflammatory diseases. Amyloidosis may involve the thyroid, gastrointestinal tract, kidneys, liver, or bone marrow. Amyloidosis as a complication of Crohn’s disease is rare but serious, and may worsen the prognosis. We have experienced a case of amyloid goiter and gastrointestinal amyloidosis secondary to Crohn’s disease. A 74-year-old female patient with Crohn’s disease was admitted to Soonchunhyang University Hospital with general weakness and poor oral intake. Anterior-neck diffuse goiter and tenderness around the navel were found. Amyloid goiter and gastrointestinal amyloidosis diagnosed by sonoguided needle biopsy of the thyroid and endoscopic biopsies of the stomach and duodenum.

Keywords: Amyloidosis; Crohn’s disease; Amyloid; Goiter; Congo red

INTRODUCTION

Amyloidosis is a disorder characterized by abnormal folding of proteins; the deposition of these proteins which compose insoluble fibrils disrupts tissue structure and function. Amyloidosis can be occurred as primary or secondary, and the deposition of amyloid fibrils can be localized or systemic [1]. Amyloidosis can be occurred secondary to chronic inflammation or chronic infection such as inflammatory bowel disease [2], rheumatoid arthritis, tuberculosis, myeloma, or bronchiectasis [3]. Amyloidosis is not common; however, it can cause serious complication in inflammatory diseases, but it is a serious complication [4,5]. It is known from clinical experience that amyloidosis only rarely appears as amyloid goiter accompanied by enlargement of the thyroid. After the first reported case of renal amyloidosis accompanying Crohn’s disease was reported in 2006 [6], a case of gastrointestinal amyloidosis accompanying Crohn’s disease was reported in 2011. In Korea, however, any case of systemic amyloidosis in Crohn’s disease diagnosed based on amyloid goiter has not been reported to-date [7]. We report here a case of secondary amyloidosis in which amyloid goiter and gastrointestinal amyloidosis occurred simultaneously in a patient with Crohn’s disease.

CASE REPORT

A 74-year-old female patient was admitted to Soonchunhyang University Hospital because of general weakness and poor oral intake. She had been diagnosed with Crohn’s disease 3 years earlier, and was being treated with 5 mg prednisolone and 3,000 mg mesalazine at the time of admission. Her abdominal pain worsened during the last 30 days. 14 days before hospitalization, we conducted abdominal computed tomography (CT), an enteroenteric fistula was observed in addition to deterioration of her Crohn’s disease. 10 days before hospitalization, we began to administer 287 mg of infliximab to the patient. Because she had been diagnosed with hypertension 6 years earlier and coronary artery disease 4 years earlier, she was taking 100 mg of aspirin, 120 mg of isosorbide dinitrate, and 90 mg of diltiazem. When hospitalized, she had a blood pressure of 120/80 mmHg, pulse of 88 beats per minute, and body temperature of 36°C. She was alert but appeared chronically ill. Unlike the follow-up observations during the previous outpatient treatment, anterior-neck diffuse goiter was found, but there was no tenderness. In the abdominal examination, it was found that the bowel sound was decreased, and there was tenderness around the navel. Laboratory examination demonstrated leukocytosis 12,000/
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Fig. 1. Thyroid sonographic findings. (A, B) Diffuse enlargement with hypoechoic texture of both thyroid glands.

Fig. 2. Thyroid computed tomography findings. Heterogeneous enhancement of both thyroids with mild enlargement.

Fig. 3. Pathologic findings. (A) Thyroid follicles surrounded by abundant pink hyaline material (H&E, ×100). (B) Positive with congo red staining (congo red stain with polarized light microscope, ×200).

mm³, hemoglobin 9.2 g/dL, platelets 142,000/µL, aspartate aminotransferase 23 U/L, alanine aminotransferase 12 U/L, Na 138 mmol/L, K 4.5 mmol/L, Cl 100 mmol/L, creatinine 1.16 mg/dL, erythrocyte sedimentation rate 48 mm/hr, and high-sensitivity C-reactive protein 22.80 mg/dL. A thyroid function test showed that T3 was 12.55 ng/dL (normal range, 60 to 190 ng/dL), free T4 1.2 ng/dL (normal range, 0.7 to 2.0 ng/dL), thyroid stimulating hormone 12.88 µIU/mL (normal range, 0.25 to 0.4 µIU/mL), thyroid stimulating immunoglobulin 0.90% (normal range, 0% to 15%), anti-thyroid peroxidase antibody 0.14 U/mL (normal range, 0 to 0.3 U/mL), and anti-thyroglobulin antibody 0.44 U/mL (normal range, 0 to 0.3 U/mL). Based on these findings, we diagnosed the patient with hypothyroidism.

By thyroid ultrasonography, diffuse hypertrophy was found in
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Fig. 4. Esophagogastrroduodenoscopic findings. (A) Endoscopy showed erythematous, edematous, and hyperemic mucosal changes in the gastric body. (B) Congo red staining of a gastric biopsy viewed under polarized light (×200). Green birefringence of interstitial amyloid deposits can be seen. (C) Endoscopy showing small ulcers with mild erythematous, edematous, and hyperemic mucosal changes in the duodenal 2nd portion (arrow: small ulcer). (D) Congo red staining of a duodenal biopsy viewed under polarized light (×200). Green birefringence of interstitial amyloid deposits is also evident.
Amyloidosis occurs when an insoluble fibrous protein, amyloid, is deposited beside cells, and may induce failure of the involved organs. As a disease related to chronic inflammation or an infectious disease, secondary amyloidosis most commonly involves the kidneys, and it also may occur in the gastrointestinal tract, liver, autonomic nerve tissue, and even the heart, albeit rarely [8]. Amyloid infiltration in the thyroid was first reported by von Rokitansky in 1855 [9]. Although amyloid was found in the thyroid of 50% to 80% of primary and secondary amyloidosis patients [10], it rarely appears clinically as diffuse goiter, which von Eisenberg named ‘amyloid goiter.’ One characteristic of amyloid goiter is its rapid growth, which makes it need to discriminate from a malignant tumor [8]. Patients with amyloid goiter rarely have thyroid dys- function, but some studies have reported cases accompanied by hyperthyroidism or hypothyroidism [11]. In this case, as the patient had thyroid goiter that occurred suddenly, and had a suspicious of a malignant tumor, we performed thyroid ultrasonography and neck CT and observed diffuse thyroid goiter on both sides. Afterward, by ultrasonography-guided needle biopsy conducted for confirmation, amyloid deposition was observed in the thyroid. Accordingly, when the thyroid is rapidly enlarged in patients with chronic inflammatory diseases, such as inflammatory bowel disease, rheumatoid arthritis, and sarcoidosis, it is necessary to determine the presence of amyloid goiter.

In this case, the patient was found to have abdominal pain and decreased ingestion, and when she was confirmed to have amyloid goiter, UGI endoscopy was carried out to find out whether amyloid involved the gastrointestinal tract. In random biopsies of both the gastric body and the duodenum, amyloid deposition was observed after congo red staining. Based on these results, the patient was diagnosed with gastrointestinal amyloidosis.

In a large-scale study of secondary amyloidosis occurring in inflammatory bowel disease, its prevalence was 0.9% in Crohn’s disease and 0.07% in ulcerative colitis. In gastrointestinal tract-involved amyloidosis, symptoms may include macroglossia, vesicular lesions, ulcers, and xerostomia in the oral cavity; motor disturbance, hematemesis, achalasia, aperistalsis, portal hypertension, and esophageal varices in the esophagus; and early satiety, nausea, vomiting, abdominal pain, and hematemesis if the stomach is involved [1,12]. The small intestine is the most common area of amyloidosis, and due to intestinal hypoperistalsis and intestinal amyloid deposition, symptoms such as diarrhea, intestinal obstruction, intestinal perforation, and intestinal bleeding can also occur [1,13]. When the large intestine is involved, amyloidosis may also cause intestinal obstruction, intestinal perforation, and intestinal bleeding [1]. As mentioned earlier, gastrointestinal amyloidosis has such varied symptoms and nonspecific findings that it is difficult to diagnose; indeed, radiologic test results and endoscopic findings are also non-specific [14]. Using a polarization microscope, congo red staining after biopsy of organs suspected of being involved will reveal an apple green color, which indicates deposition of amyloid fibroid material.

One of the principles of treatment of secondary amyloidosis is to reduce the creation of serum amyloid A protein [15]. No effective treatment has yet been developed, but it has been reported that inflammation-suppressive or immunosuppressive therapies, mainly using tumor necrosis factors such as cytokines, are efficacious [16]. In this case, the patient with Crohn’s disease had deteriorated, and an enteroenteric fistula was discovered, so infliximab was administered. After this, we were diagnosed with amyloidosis. After the patient had been diagnosed with amyloidosis, it was planned that infliximab would be administered again, but because of the general deterioration due to sepsis, this did not occur.

Amyloidosis accompanying Crohn’s disease is rare, and its symptoms and endoscopic findings are non-specific, which may delay diagnosis. Amyloidosis can involve several organs such as the kidney, gastrointestinal tract, heart, liver, and thyroid, and when a patient receives treatment lately the prognosis may be poor. Therefore, it is necessary to confirm symptoms attentively during follow-
up observations, and when abnormal findings are found in a physical examination such as cervical goiter, specific tests should be carried out to determine whether systemic amyloidosis is present.

REFERENCES

1. Sattianayagam PT, Hawkins PN, Gillmore JD. Systemic amyloidosis and the gastrointestinal tract. Nat Rev Gastroenterol Hepatol 2009;6:608-17.
2. Schmidt H, Riemann JF. Amyloidosis in Crohn disease. Dtsch Med Wochenschr 1983;108:795-7.
3. Rashid H, Blake D, Gokal R, Gooptu D, Kerr DN. The association of renal amyloidosis with regional enteritis (Crohn’s disease): report of two cases and review of the literature. Clin Nephrol 1980;14:154-7.
4. Greenstein AJ, Sachar DB, Panday AK, Dikman SH, Meyers S, Heimann T, et al. Amyloidosis and inflammatory bowel disease: a 50-year experience with 25 patients. Medicine (Baltimore) 1992;71:261-70.
5. Wester AL, Vatn MH, Fausa O. Secondary amyloidosis in inflammatory bowel disease: a study of 18 patients admitted to Rikshospitalet University Hospital, Oslo, from 1962 to 1998. Inflamm Bowel Dis 2001;7:295-300.
6. Jin GB, Yoon JS, Lee KT, Hwang EA, Han SY, Park SB, et al. A case of secondary renal amyloidosis complicating Crohn’s disease. Korean J Med 2006;70:309-12.
7. Park KT, Kang DH, Choi CW, Park SB, Lee JH, Kim BG, et al. A case of gastrointestinal amyloidosis as a complication of Crohn’s disease. Korean J Gastrointest Endosc 2011;42:401-5.
8. Gertz MA, Kyle RA. Secondary systemic amyloidosis: response and survival in 64 patients. Medicine (Baltimore) 1991;70:246-56.
9. Von Rokitansky C. Allgemeine pathologische Anatomie und anomalien des Blotes. In: von Rokitansky C, editor. Lehrbuch der pathologischen Anatomie. Wien: Braumuller; 1855. p. 326-8.
10. Bell GO, Mena BA. Amyloid goiter associated with the nephrotic syndrome. Med Clin North Am 1963;47:385-9.
11. Kimura H, Yamashita S, Ashizawa K, Yokoyama N, Nagataki S. Thyroid dysfunction in patients with amyloid goitre. Clin Endocrinol (Oxf) 1997;46:769-74.
12. Menke DM, Kyle RA, Fleming CR, Wolfe JT 3rd, Kurtin PJ, Oldenburg WA. Symptomatic gastric amyloidosis in patients with primary systemic amyloidosis. Mayo Clin Proc 1993;68:763-7.
13. Hayman SR, Lacy MQ, Kyle RA, Gertz MA. Primary systemic amyloidosis: a cause of malabsorption syndrome. Am J Med 2001;111:535-40.
14. Moon W, Lee OY, Cho YJ, Yang SY, Park HY, Han SH, et al. The endoscopic findings and clinical characteristics of gastrointestinal amyloidosis. Korean J Gastrointest Endosc 2005;31:216-20.
15. Gillmore JD, Lovat LB, Persey MR, Pepys MB, Hawkins PN. Amyloid load and clinical outcome in AA amyloidosis in relation to circulating concentration of serum amyloid A protein. Lancet 2001;358:24-9.
16. Park YK, Han DS, Eun CS. Systemic amyloidosis with Crohn’s disease treated with infliximab. Inflamm Bowel Dis 2008;14:431-2.