A Case of Amyloid Goiter Secondary to Crohn's Disease

SATOSHI HABU*, HAJIME WATANOBE*, KEN-ICHI KIMURA**, AND TOSHIHIRO SUDA*

*Third Department of Internal Medicine, Hirosaki University School of Medicine, Hirosaki, Aomori 036, and **Division of Endocrinology, Aomori Prefectural Central Hospital, Aomori, Aomori 030, Japan

Abstract. We herewith report a case of amyloid goiter secondary to Crohn's disease. The patient had been diagnosed as having Crohn's disease at the age of 15, and underwent right hemicolectomy at age 20. When he was 26 years old he complained of swelling of the anterior neck. Both TSH and thyroid hormones were within the normal range, and anti-thyroglobulin and anti-microsomal antibodies were negative. Only thyroglobulin was noticeably above the normal range. During the next year his goiter enlarged further and because he had a feeling of pressure he underwent total thyroidectomy. The presence of amyloid A protein in his surgical specimen led to the diagnosis of amyloid goiter. Although most cases of secondary amyloidosis are known to develop in neoplasms or chronic inflammatory diseases, our patient had no illness other than Crohn's disease. Perusal of literature revealed that Crohn's disease is rarely a cause of amyloid goiter.

Key words: Amyloid goiter, Crohn's disease, Secondary amyloidosis

AMYLOIDOSIS is usually broadly classified as primary or secondary, and in the majority of cases secondary amyloidosis is caused by neoplasms or chronic inflammatory diseases. In 1948, Olson et al. [1] reported the first case of secondary amyloidosis caused by Crohn's disease. Although inflammatory bowel disease (IBD) is rarely complicated by amyloidosis, the majority of such patients with secondary amyloidosis suffer from Crohn's disease [2, 3]. Most cases of secondary amyloidosis are discovered by proteinuria or nephrotic syndrome due to renal amyloidosis, and only a minor proportion of the patients show clinical symptoms due to other organ involvement. Although amyloid is often found deposited in the thyroid gland at autopsy and in surgical specimens [4], it is clinically rare to see the thyroid gland obviously enlarged or for thyroid function to become abnormal [5, 6].

We recently saw a rare case of amyloid goiter that developed 11 years after the onset of Crohn's disease. We herewith report the details of the patient's condition and add a discussion.

Case Report

In 1984 a 15-year-old boy was diagnosed as having Crohn's disease and was treated with salazosulfapyridine orally. In 1989 at age 20, since he developed abdominal pain and diarrhea and his barium study and colonoscopy findings did not improve, he underwent right hemicolectomy. After that operation, although symptoms often developed, they were controlled by salazosulfapyridine and prednisolone. In June, 1995 at age 26, the patient was first seen at our clinic complaining of swelling of the anterior neck. His thyroid gland was enlarged, nodular, firm and non-tender. The size of the right lobe was 9.0 × 4.0 cm and the left was 8.5 × 3.0 cm. His laboratory data showed microcytic hypochromic anemia,
hypoalbuminemia and hypolipidemia, and his renal function was normal except that his urinary protein was slightly positive. Free T₃, free T₄ and TSH were all within the normal range. Anti-thyroglobulin and anti-microsomal autoantibodies were negative. Thyroglobulin (Tg), which was the only abnormal thyroid function test, was noticeably above normal (625 ng/ml; normal, < 30 ng/ml, Table 1). On ultrasonography (US), because there were areas with different echo levels consistent with cystic lesions of various sizes in his thyroid gland, we made a diagnosis of adenomatous goiter (Fig. 1). The results of computed tomography (CT) were also compatible with adenomatous goiter. Thereafter, because he did not have symptoms of anterior neck compression, he was clinically followed up without treatment. In August, 1996, since he began to complain of an oppressive feeling in the anterior neck and his goiter was further enlarged, a total thyroidectomy was performed. Histologically, follicles were sparse and cysts were dispersed all through the thyroid gland. Hematoxylin and eosin staining revealed abnormal extracellular eosinophilic deposits. This substance stained positive with Congo red (Fig. 2a) and turned negative after pretreatment with potassium-permanganate prior to the same stain (Fig. 2b). We therefore diagnosed this substance as amyloid A protein. There were neither malignant nor inflammatory cells. After total thyroidectomy, we needed to give him 250 μg per day of levothyroxine in order to normalize the levels of thyroid hormone and TSH.

To evaluate other organs, rectal biopsy was performed, but there was no amyloid deposition. Although renal biopsy was not carried out, renal amyloidosis was suspected because blood urea nitrogen and creatinine began to rise gradually and urinary protein has been obviously positive since 1996.

**Discussion**

Secondary amyloidosis is generally caused by malignant tumors or chronic inflammatory diseases, most often rheumatoid arthritis (RA). In 1948, Olson et al. [1] reported a case of secondary amyloidosis caused by Crohn's disease. Thereafter, some similar cases and reviews have occasionally been reported. According to these reports, in 1–8% of patients Crohn's disease can be complicated by amyloidosis [2, 3]. In 1992 Greenstein et al. [7] further investigated 3,050 patients with IBD in detail. In that report, there were 25 patients (0.82%) whose IBD was complicated by secondary amyloidosis, 22 of 1708 patients with Crohn's disease having amyloidosis, and 3 of 1342 patients

**Table 1.** Endocrinological data

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Free T₃</td>
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</tr>
<tr>
<td>Free T₄</td>
<td>1.2 ng/ml</td>
</tr>
<tr>
<td>TSH</td>
<td>2.5 μU/ml</td>
</tr>
<tr>
<td>Thyroid test</td>
<td>&lt;100 ×</td>
</tr>
<tr>
<td>Microsome test</td>
<td>&lt;100 ×</td>
</tr>
<tr>
<td>TSH receptor antibody</td>
<td>negative</td>
</tr>
<tr>
<td>Thyroglobulin</td>
<td>625 ng/ml</td>
</tr>
<tr>
<td>Anti-thyroglobulin antibody</td>
<td>&lt;0.3 IU/ml</td>
</tr>
<tr>
<td>Calcitonin</td>
<td>17 pg/ml</td>
</tr>
</tbody>
</table>

**Fig. 1.** Ultrasonography of the thyroid. a) axial section. b) longitudinal section. In his thyroid gland there were areas with different echo levels consistent with cystic lesions of various sizes.
AMYLOID GOITER SECONDARY TO CROHN'S DISEASE

with ulcerative colitis having the same complication. As to the main clinical manifestations of amyloidosis, 21 patients had kidney involvement, 3 had intestinal involvement, and one had heart and one had thyroid involvement. Meyers et al. [8] reported that 29.4% of patients with Crohn's disease had renal amyloidosis at autopsy, but only 1% were diagnosed during life. Most cases of secondary amyloidosis are discovered by proteinuria or nephrotic syndrome due to renal amyloidosis [9]. In our patient, when he was first seen at our clinic in 1995, his laboratory data showed hypoalbuminemia. Since his blood urea nitrogen and creatinine were normal and urinary protein was slightly positive, renal biopsy was not performed. Although the presence of renal amyloidosis could not be ruled out at that time, he was thought to be undernourished due to malabsorption because he had undergone ileotomy and Crohn's disease still persisted in his ileum. The fact that he needed a larger than normal dosage of levothyroxine after total thyroidectomy, may be explainable by his malabsorption state.

In the report by Greenstein et al. [7], there were 5 patients (0.16%) with amyloid deposition in the thyroid gland at biopsy or autopsy, and only one among them having had a clinical manifestation. Although it was reported that amyloid deposition was found in 50% of primary amyloidosis and 80% of secondary amyloidosis in surgical specimens or at autopsy [4], it is said to be comparatively rare for goiter and abnormal thyroid function to be found [2, 5], but Kimura et al. [10] recently reported that abnormalities of the thyroid gland were seen with a higher incidence than in previous reports [5]. According to Kimura et al. [10], goiter was found in 63% of patients with secondary amyloidosis, and various thyroid dysfunctions were found in 90% of patients with goiter, which included hypothyroidism, hyperthyroidism and transient thyrotoxicosis. They reported that in all patients with goiter Tg was higher than normal with or without thyroid dysfunction. It is likely that Tg may increase due to destruction of thyroid follicles by amyloid deposition.

In our patient, we first made a diagnosis of adenomatous goiter based upon US and CT findings. In a previously reported case of amyloid goiter which was complicated by fatty infiltration, the thyroid US showed a high echogenicity [11]. In turn, Fontan et al. [12] reported several cases of amyloid goiter in which cystic and solid lesions coexisted, which, on a morphological basis, can be reasonably diagnosed as adenomatous goiter similar to our case. In our patient, the existence of amyloid A protein in the thyroid was confirmed, and there were no neoplasms or other inflammatory diseases other than Crohn's disease. We therefore consider the patient as another rare case of amyloid goiter developed in Crohn's disease.

The preexisting literature reported that thyroid involvement is rare as a clinical manifestation of secondary amyloidosis, but we learned from our experience with this patient that it may be advisable to examine the thyroid gland for goiter and to monitor thyroglobulin in addition to renal function,
in order to detect secondary amyloidosis at an early stage in the follow-up of patients with chronic inflammatory diseases, such as IBD and RA. Furthermore, if the thyroid gland is enlarged or thyroglobulin is high, we should monitor thyroid function.

References