Multiple Branchial Cleft-Like Cysts in a Female Patient with Hashimoto's Thyroiditis

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Abstract. We report a case of branchial cleft-like cysts (intrathyroidal lymphoepithelial cysts) associated with Hashimoto's thyroiditis. Palpation did not detect any nodules. Multiple cystic lesions were detected in the lateral side of the thyroid bilateral lobes by imagings of an I-123 scintigram, Tl-201 scintigram, sonography, and computerized tomography. Sonography displayed multiple cysts with strong echogenic spots in the cystic fluid. Repeated fine needle aspiration biopsies of the cysts consistently revealed only normal lymphocytes. Although these lesions could not be given diagnosis, subtotal thyroidectomy leaving the intact isthmus was performed. Microscopic findings revealed multiple branchial cleft-like cysts lined by flattened epithelial cells. Surrounding the epithelial lining were dense lymphoid follicles with large, reactive germinal centers. The remaining thyroid parenchyma showed Hashimoto's thyroiditis. Multiple branchial cleft-like cysts should be considered when sonographic examination reveals multiple cysts in the lateral side of the bilateral lobes, and fine needle aspiration biopsy displays only normal lymphocytes. To our knowledge, this is the first case of branchial cleft-like cysts associated with Hashimoto's thyroiditis reported in Japan.

Key words: Hashimoto's thyroiditis, Lymphoepithelial cysts, Multiple branchial cleft-like cysts, Solid cell nests

MULTIPLE branchial cleft-like cysts (intrathyroidal lymphoepithelial cysts) with histopathological features resembling those of branchial cleft cysts have been reported in the thyroid gland [1–3]. The cysts have a squamous but sometimes columnar epithelial lining with abundant underlying lymphoid tissues, including lymphoid aggregates with large reactive germinal centers. The origin of multiple branchial cleft-like cysts remains to be clarified. Some investigators speculate that branchial cleft cysts are the origin of multiple branchial cleft-like cysts, based on their histopathological similarities [4, 5]. Branchial cleft cysts, which are characterized by swelling in the upper third of the lateral neck anterior to the sternocleidomastoid muscle [4], have also been reported to be located at unusual sites, such as oral cavity, parotid gland, and pancreas [6–8]. The histogenesis of branchial cleft cysts is unclear, but is generally assumed to be a developmental abnormality originating from branchial cleft remnants. On the other hand, solid cell nests (SCNs), which were disclosed to be of ultimobranchial body origin [9–12], were considered alternatively to be the origin of multiple branchial cleft-like cysts [2]. In SCNs, small microscopic cystic structures containing mucinous materials were commonly present [9, 10]; this suggests that they could be the origin of multiple branchial cleft-like cysts. We report multiple branchial cleft-like cysts in a patient with Hashimoto's thyroiditis. To our knowledge, this is the first case reported in Japan.

Received: June 18, 1999
Accepted: March 24, 2000
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Case Report

A 36-year-old Japanese woman who had noticed neck swelling for the past 4 months was referred to our department. The goiter was large with a smooth surface and without palpable nodules. The right lobe was measured at $5.5 \times 2.8$ cm, the left lobe at $4.5 \times 2.5$ cm. Her thyroid function was normal. Antithyroglobulin antibody measured by a commercially available hemagglutination kit (Fuji Rebio, Tokyo) was negative ($< 100$ times), and 26 IU/ml by a sensitive radioassay (Eiken Chemical Co., Tokyo) (normal $< 70$ IU/ml). The titer of an antithyroid microsomal antibody measured by the hemagglutination assay (Fuji Rebio, Tokyo) was 100 times (normal $< 100$). The trachea was shifted to the left on a neck X-ray examination. I-123 scintigram displayed heterogeneous distribution of radioactivity mixed with several cold and warm areas (Fig. 1). Cold nodules were supposed to be located in the lower two-thirds of the right lobe, and in the upper third and lower third of the left lobe. T1-201 scintigram showed cold nodules in the bilateral lobes at the same location as that shown in I-123 scintigram. Sonography revealed 2 large cysts in the right lobe, 3 large cysts in the left lobe, and several other small cysts in the bilateral lobes. The location and the size of the cysts were as follows: the upper third of the right lobe, $2.1 \times 1.7$ cm; the lower two-thirds of the right lobe, $4.3 \times 3.2$ cm; the upper third of the left lobe, $2.5 \times 1.7$ cm; the middle third of the left lobe, $2.0 \times 1.7$ cm; and the lower two-thirds of the left lobe, $3.5 \times 2.9$ cm. Each cyst had a smooth, discrete wall with several septa. Their lumens were heterogeneous with strong echogenic spots (Fig. 2). These spots of echogenicity were supposed to be caused by suspended debris in the cysts. On computerized tomography images, cysts appeared to be discrete smooth-walled homogeneous hypodensity lesions surrounded by a rim of compressed normal thyroid tissue. No enhancement was observed in the cysts, while the compressed portions of the thyroid gland in the bilateral lobes and the isthmus were enhanced after contrast injection (Fig. 3). Fine needle aspiration cytology of the right lower and the left lower cysts, which was performed 3 times, consistently revealed only normal lymphocytes in a small amount of clear fluid. No follicular epithelium or foamy cells were observed in any sample obtained. The diagnosis of adenomatous nodules with cystic changes...
concomitant with Hashimoto's thyroiditis was highly suspected. However, the cytological findings were atypical of adenomatous nodules. Subtotal thyroidectomy leaving the intact isthmus was performed. The postoperative course was uneventful and the patient's thyroid function was normal after 60 months with treatment of levothyroxine sodium at 125 µg a day.

**Pathological findings**

**Gross findings**

The right lobe specimen was 6.0 × 3.5 cm in size with a smooth external surface. It contained light-brown cysts. The left lobe specimen measured 6.0 × 3.0 cm and the appearance was essentially identical to that from the right lobe. The cysts contained yellow viscous fluid. The largest cyst was 4.3 × 3.2 cm in size. The granular cobblestone appearance with a white thin wall was observed in the inner surface of the cysts (Fig. 4).

**Microscopic findings**

The size of the cysts was variable, but the microscopic characteristics of all cysts were essentially the same. Each cyst was lined by a predominantly flattened epithelium ranging from one to two cells in thickness (Figs. 5, 6). Surrounding the epithelial lining were dense lymphoid follicles with large reactive germinal centers. The cysts were not clear-
ly separated from the adjacent thyroid tissues, although fibrous tissue was focally observed between cyst walls and thyroid tissues. The thyroid parenchyma showed atrophy oxyphilic cell change, and diffuse lymphocystic infiltration with lymphoid follicle formation, all of which indicate characteristic features of Hashimoto’s thyroiditis (Fig. 7).

Immunohistochemically, the epithelial lining of the cysts was strongly immunoreactive for keratin, but not reactive for thyroglobulin or CEA.

Discussion

Given that the number of reported cases of multiple branchial cleft-like cysts is very small and that the clinical characteristics of this disease are not yet clarified, it is difficult to make a diagnosis of branchial cleft-like cysts solely based on clinical examinations. Most cystic lesions of the thyroid develop as a result of degeneration in a nodular goiter or a neoplasm. These cysts are usually lined by squamous epithelia. The differentiation from multiple branchial cleft-like cysts can be based on the location in the thyroid gland, as well as the distinct cytological findings of the specimen obtained by fine needle aspiration biopsy. We stress that multiple branchial cleft-like cysts should be considered when sonographic examination reveals multiple cysts in the lateral side of the thyroid gland, and a fine needle aspiration cytology detects only normal lymphocytes.

Some controversy remains over the origin of branchial cleft-like cysts of the thyroid gland. Recent studies revealed the possibility that SCNs are the origin of clinically detected lymphoepithelial cysts, because SCNs are mainly located in the middle third of the bilateral lobes and are not found in the isthmus [12], which corresponds to the site of predilection for clinically detectable branchial cleft-like cysts. On the other hand, microscopic studies show two cell types forming SCNs [11]. One of these cells, named as the “main cell”, shows positive immunohistochemical staining for high and low molecular weight keratins and CEA in most cases, and negative staining for thyroglobulin [9-12]. These findings are similar to those found in immunohistochemical studies of the epithelial cells of multiple branchial cleft-like cysts which showed positive for keratin and negative for thyroglobulin. However, the epithelial cells of the cysts were negative for CEA in some reported cases, as in this one. In addition, the role of thyroid autoimmunity, which is frequently seen in multiple branchial cleft-like cysts [1, 2], has not been clarified in branchial cleft-like cysts. Further investigation is necessary to determine the origin and the mechanism of formation of multiple branchial cleft-like cysts. The result of immunohistochemical staining in this case did not support the hypothesis that SCNs are the origin of multiple branchial cleft-like cysts.

References


