Sarcoid Reaction in Thyroid Diseases: Report of a Case of Thyroid Carcinoma Demonstrating Sarcoid Reaction in Regional Lymph Nodes

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Abstract. We describe an extremely rare case of thyroid carcinoma accompanied by sarcoid reaction in regional lymph nodes. The patient, a 40-year-old woman, was found to have anterior neck swelling during a routine medical examination. Physical examination revealed a bad movable and firm nodule measuring 3.5 x 2.5 cm in the right thyroid lobe. Examination of a fine-needle aspiration cytology of the nodule suggested papillary carcinoma of class V. Right lobectomy and isthmectomy with neck dissection were performed. Histopathological examination of the resected specimens revealed papillary carcinoma accompanied by metastatic foci in right perithyroidal lymph nodes and non-caseous sarcoid-like granulomas in pretracheal, right upper internal deep cervical and submandibular lymph nodes. We concluded that these granulomas were due to a sarcoid reaction associated with thyroid carcinoma, after performing examinations to rule out the possibility of systemic sarcoidosis.

Key words: Sarcoid reaction, Thyroid carcinoma

EPITHELIOD cell granulomas identical to those of systemic sarcoidosis are occasionally observed within primary foci or regional lymph nodes in malignant tumors [1]. Such histological changes which are not indicative of systemic sarcoidosis are called sarcoid reactions [2]. This report describes an extremely rare case of thyroid carcinoma accompanied by sarcoid reaction in regional lymph nodes. We also discuss the significance of sarcoid reaction in thyroid diseases.

Case Report

The patient, a 40-year-old woman, was found to have anterior neck swelling during a routine medical examination. Physical examination revealed a bad movable and firm nodule measuring 3.5 x 2.5 cm in the right thyroid lobe. No abnormalities were noted in general hematology or blood biochemistry tests. Serum TSH, free T3 and free T4 were within the normal range (1.76 µU/ml, 1.37 ng/dl, and 4.8 pg/ml, respectively). Serum thyroglobulin was slightly high (32 ng/ml). Antithyroid autoantibody to thyroglobulin was positive (10%) and that to thyroid microsomal antigen was also positive (×6400). Examination of a fine-needle aspiration cytology of the nodule suggested papillary carcinoma of class V. Right lobectomy and isthmectomy with neck dissection were performed because the right upper internal deep cervical and submandibular lymph nodes were found to be swollen intraoperatively. Histopathological examination of the resected thyroid specimens revealed papillary carcinoma...
invading to the surrounding thyroid tissue accompanied by intraglandular metastases and chronic thyroiditis (Fig. 1). Histopathological examination of the resected lymph node specimens revealed metastatic foci in right perithyroidal nodes and non-caseous sarcoid-like granulomas in pretracheal, right upper internal deep cervical and submandibular nodes (Fig. 2). To rule out the possibility of systemic sarcoidosis, the following examinations were performed after the operation. Chest x-ray and computed tomography films showed no abnormal findings in the lung field or mediastinum. Tuberculous skin test with purified protein derivative showed 15 x 10 mm swelling and 71 x 50 mm erythema. The serum total protein level was 7.1 g/dl, with 66.54% albumin, 4.10% $\alpha$1-globulin, 7.40% $\alpha$2-globulin, 7.53% $\beta$-globulin, and 14.40% $\gamma$-globulin. The blood white cell count was 5100/mm$^3$, with 2% stab cells, 60% segmented cells, 1% eosinophils, 35% lymphocytes, and 2% monocytes. Serum angiotensin converting enzyme, lysozyme and calcium levels were within the normal range (9.8 IU/l at 37 °C, 4.0 g/ml and 9.4 mg/dl, respectively). Ophthalmologic examinations in the anterior chamber, anterior chamber angle and ocular fundus showed no abnormalities. Based on these findings, the possibility of systemic sarcoidosis was excluded and we therefore concluded that these granulomas were due to a sarcoid reaction associated with thyroid carcinoma. Four years have passed since the operation, and the patient is doing well, without any signs of recurrence.

Discussion

Since Nickerson first pointed out the difference between sarcoid reaction associated with malignant tumors and systemic sarcoidosis in 1937 [2], sarcoid reaction has been reported in various types of malignant tumors [1]. Such sarcoid reaction has also been found associated with infectious diseases such as tuberculosis, chemical agents such as beryllium, immunodeficient states such as primary biliary cirrhosis autoimmune diseases such as chronic thyroiditis and Basedow's disease, and diseases of unknown cause such as Crohn's disease [1, 3-5].

Brincker [1] reviewed data on 4020 patients with malignant tumors in a broad spectrum. He found that 165 (4.4%) of 3770 patients with carcinomas and one (0.4%) of 250 patients with sarcomas had sarcoid reactions. Sarcoid reaction may be slightly more common in patients with squamous cell carcinomas than in those with adenocarcinomas. Sarcoid reaction has been observed in many kinds of primary tumors and particularly in regional lymph nodes, regardless of the presence of lymph node metastases but sarcoid reaction occurred about four times more often in regional lymph nodes without metastases than in lymph nodes with concomitant metastases. Rarely, sarcoid
reaction has also been found in distant metastases, in lymph nodes regional to distant metastases and in non-involved organs, such as the spleen.

To our knowledge, only five cases of sarcoid reaction associated with thyroid carcinomas have been reported in the literature [6-9]. There have been four cases of sarcoid reaction associated with thyroid carcinomas reported in Japan, but the reason why Japanese accounted for the majority is not known. All 5 cases were demonstrated to have sarcoid reactions in the regional lymph nodes [6-9]. One had a sarcoid reaction in the thyroid gland and the regional lymph nodes [9], and another had it in the thyroid gland, regional lymph nodes and anterior cervical skin [8]. In all 5 cases, it was difficult to detect the sarcoid reaction in either the thyroid gland or regional lymph nodes, both preoperatively and intraoperatively [6-9]. Although an intraoperative frozen section may be helpful in detecting the existence of sarcoid reaction intraoperatively, it was not attempted in any of the 5 cases [6-9]. Moreover, sarcoid reaction in the thyroid gland manifested as the primary focus of thyroid carcinoma, whereas in the regional lymph nodes it was mistaken for metastatic lymph nodes from the macroscopic findings intraoperatively. Consequently, over surgery might have been performed to completely resect the suspected carcinoma tissue. The prognostic significance of sarcoid reaction in thyroid carcinoma has not been determined, because the prognosis of well differentiated thyroid carcinoma is, in general, just as good. On the other hand, sarcoid reaction might be associated with a better prognosis in other malignant tumors, because it may be a marker of an immunologically mediated antitumor response of macrophages activated by T cells [1, 10].

It is sometimes difficult to differentiate sarcoid reaction related to thyroid diseases from systemic sarcoidosis associated with thyroid diseases [11, 12]. Sarcoid reactions associated with several types of thyroid diseases such as thyroid carcinoma [6-9], benign thyroid nodules, malignant lymphoma of the thyroid [11], chronic thyroiditis and Basedow’s disease [5], were found in the thyroid gland or the regional lymph nodes of the thyroid gland. Two major factors, namely, thyroid tumor and autoimmune thyroid disease, must be taken into consideration when discussing the characteristics of sarcoid reactions in thyroid diseases. The pathogenesis of sarcoid reactions is uncertain and they are, in general, supposed to be the result of a latent immunological abnormality. Sarcoid reactions associated with a thyroid tumor may be caused by some immunological reactions of the host against a metabolic product or resolvent derived from the tumor cells [2]. Although the relationship between the degree of autoimmune diseases and the appearance of sarcoid reactions has never been discussed, sarcoid reactions associated with autoimmune thyroid diseases may be based on an autoimmune disturbance resulting from loss of T cell control [13]. Our case also had both two factors, namely, thyroid tumor and autoimmune thyroid disease, and so the pathogenesis may be explained by a latent immunological abnormality in either factor.

References


