

RESEARCH COMMUNICATION

Normal CA 19-9 Levels in Hashimoto's Thyroiditis

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Abstract

Carbohydrate antigen 19-9 (CA 19-9) is a glycosphingolipid of the Lewis blood group that for years has been proposed as a useful marker for epithelial type gastrointestinal cancers. It is well known that moderately increased concentrations of CA 19-9 can be found in 15-36 % of patients with benign conditions such as pancreatic, liver, biliary diseases and benign hydronephrosis. In current study, we investigated whether there was any tendency for CA 19-9 elevation in 71 patients with Hashimoto's thyroiditis. Patients with malignancy, benign pancreas, liver, lung and biliary diseases, inflammatory bowel diseases, urinary tract infection, hydronephrosis, endometriosis, diabetes mellitus and chronic renal failure were excluded. In the Hashimoto's thyroiditis cases, mean serum CA 19-9 level was 12.5 ± 10.4 (range, 2.5-55), while it was 11.9 ± 9 (range, 2.5-29.3) and 10.3 ± 8 (range, 2.5-28.9) in patients with Graves' and healthy volunteers respectively, without any significant intergroup differences. Although the American Society of Clinical Oncology does not recommend tumor markers like CA 19-9 in screening for malignancies, they may be used for this purpose. In contrast to case reports showing possible elevation of CA 19-9 in Hashimoto's thyroiditis, we did not detect such a relation. Moreover, there was no pointers to change in CA 19-9 levels in patients with hypo-, hyper- or eu-thyroidism.

Key Words: Hashimoto's thyroiditis - CA 19-9 - tumour marker

Asian Pacific J Cancer Prev, 10, 315-318

Introduction

Carbohydrate antigen 19-9 (CA 19-9) is a glycosphingolipid of the Lewis blood group that for years has been proposed as a useful marker for epithelial type gastrointestinal cancers, especially those of the pancreas and biliary tract. The sensitivity of CA 19-9 for the diagnosis of pancreatic adenocarcinoma has been reported as 81% with a specificity of 90% using a cut-off level of 40 U/mL (Katsanos et al., 2002). High CA 19-9 levels have been associated with unresectable lesions and a poor prognosis for patients presenting with pancreatic carcinoma (McLaughlin et al., 1999; Parra et al., 2005). CA 19-9 expression has been demonstrated in various normal tissues including the gall bladder, pancreas, stomach, colon, bronchial tree, endometrium, salivary glands and prostate (Akdogan et al., 2001; Parra et al., 2005; Aybek et al., 2006). It is well known that moderately increased concentrations of CA 19-9 can be found in 15-36% of patients with benign conditions such as pancreatic, liver and biliary diseases (Collazos et al., 1992; McLaughlin et al., 1999; Akdogan et al., 2001; Katsanos et al., 2002; Berger et al., 2004; Kim et al., 2004; Parra et al., 2005) and benign hydronephrosis (Aybek et al., 2006). Thyroid disorders affect many organs including the central nervous system, the gastrointestinal system and the

cutaneous system. In the literature, there are also some reports pointing to a relation between Hashimoto's thyroiditis and elevated levels of serum CA 19-9 (Schmid et al., 1992; Parra et al., 2005).

In current study, we aimed to investigate whether there was any tendency CA 19-9 elevation in Turkish patients with Hashimoto's thyroiditis.

Materials and Methods

Seventy one patients with diagnosis of Hashimoto's thyroiditis were included in the study. Hashimoto's thyroiditis defined as hypothyroidism together with the presence of at least one of thyroid autoantibodies. Thyroid ultrasonography was done in all patients with Hashimoto's thyroiditis. All patients were non-smokers. Patients with malignancy, benign pancreas, liver, lung and biliary diseases, inflammatory bowel diseases, urinary tract infection, hydronephrosis, endometriosis, diabetes mellitus and chronic renal failure were excluded from the study.

The controls were two groups of patients: in the first group 35 patients with Graves' disease and in the second 35 completely normal healthy volunteers. The control groups were similar with regard to age and sex.

Local ethical committee of Mersin University

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approved this study. Aim of study was explained to all women and written consent was obtained from all. Demographic characteristics including sex, age and drug history for levothyroxine or anti thyroid drug were recorded carefully.

Blood Hormone Analyses

Biochemical samples for TSH, fT3, fT4, anti-Tg, anti-TPO and CA 19-9 were obtained in the morning between 0800 and 0900 h. Serum TSH, free T4, anti-thyroid peroxidase antibody (anti-TPO) and anti-thyroglobulin antibody (anti-Tg) levels were measured by Moduler E170 (Roche Diagnostic, Mannheim, Germany). Euthyroidism was defined as normal TSH values (0.3-4.5 mIU/L) and free T4 (10-22 pmol/L). Thyroid autoimmunity was defined as serum levels of either antithyroid peroxidase or antithyroglobulin antibodies higher than 12 and 34 IU/mL, respectively.

Serum CA 19-9 levels (normal levels 0-27 U/mL) were measured by competitive electrochemiluminescence method (Moduler E170, Roche Diagnostic, Mannheim, Germany).

Statistical Analysis

All statistical analysis was performed by using the software SPSS version 16 packet programs (SPSS Inc., Chicago, IL.). Descriptive statics are used as mean \pm standard deviations. Comparisons between groups were made by using the independent samples t test. Pearson correlation analysis was used to determine the correlations between clinical characteristics. P values lower than 0.05 were considered statistically significant.

Results

Of the 71 patients with Hashimoto's thyroiditis, 60 (84.5%) were female. The mean age was 43.8 \pm 14.4 years old.

There was no significant difference between Hashimoto's thyroiditis and control groups with regard to the serum CA 19-9 levels (see Table 1), or between hypo- and euthyroid patients among Hashimoto's thyroiditis cases. We could not detect any relation between serum CA 19-9 levels and TSH levels or thyroid autoantibody (anti-TPO and anti-Tg) levels.

Discussion

Serum CA 19-9 levels are widely accepted tumor marker of gastrointestinal system tumors especially pancreatic adenocarcinoma. It is detected by a monoclonal antibody that recognizes certain carbohydrate groups

Table 1. Serum CA 19-9 Levels in Patient and Control Groups

Patients	CA 19-9 levels (U/ml) (range)
Hashimoto's thyroiditis	12.5 \pm 10.4 (2.5-52.9)
Hypothyroid	13.2 \pm 10.9 (2.5-52.9)
Euthyroid	10.5 \pm 9.0 (2.5-28.9)
Graves disease (control group 1)	11.9 \pm 9.0 (2.5-29.3)
Normal (control group 2)	10.3 \pm 8.0 (2.5-28.9)

newly shed from the surface of the pancreatic cells by the action of abnormal glycosyltransferases which are activated during oncogenic transformation (Andren-Sandberg, 1989). Usually, CA 19-9 levels above 1000 U/mL are associated with malignant disease (Ritts, Del Villano et al. 1984). However, it was shown that some benign disorders including chronic liver diseases (Collazos et al., 1992; Sohda et al., 1998; Montalto et al., 2005; Calisto et al., 2008), collagen vascular diseases (Safadi et al., 1998; Szekanecz et al., 2007; Szekanecz et al., 2008), inflammatory bowel diseases and hydronephrosis (Aybek et al., 2006) may also cause elevated levels of serum CA 19-9. In literature, there are also some reports indicating that Hashimoto's thyroiditis may be another benign cause of CA 19-9 elevation. The proposed mechanism was that tumor-associated antigens (TAAs), in addition to the cancer cells, may be expressed on the surface of inflammatory cells and these TAAs may play a role in the continuation of inflammation.

In the current study, we found no significant elevations in serum CA 19-9 levels in patients with hypothyroidism compared with hyper- and euthyroid women. Moreover, in subgroup analyses of patients with Hashimoto's thyroiditis, we found no significant difference in CA 19-9 levels according to euthyroidism or hypothyroidism status. As we have found, Hashimoto et al (1990) reported that no differences among hypo-, hyper and euthyroid patients. Although CA 19-9 is not expressed by normal thyroid tissue, it is occasionally observed in patients with various thyroid gland pathologies, supporting the inflammatory cells shedding theory (Vierbuchen et al., 1989; Hashimoto et al., 1990; Schmid et al., 1992). In a study investigating the CA 19-9 expression in thyroid gland pathologies including subacute thyroiditis, Hashimoto's thyroiditis and thyroid cancers showed a weak CA 19-9 expression in patients with Hashimoto's thyroiditis (Schmid et al., 1992). Moreover, the strongest CA 19-9 expression was observed in patients with late stage subacute thyroiditis and in papillary carcinomas with marked sclerosis. However, we did not detect any significant difference in patients with chronic autoimmune thyroiditis and healthy control. Moreover, there was no relation between thyroid autoantibody levels and CA 19-9 levels.

In the literature there are some reports showing autoimmune processes including rheumatoid arthritis (Szekanecz et al., 2007), systemic lupus erythematosus (Szekanecz et al., 2008), scleroderma, the Sjögren syndrome (Safadi et al., 1998) and autoimmune hepatitis (Sohda et al., 1998; Montalto et al., 2005; Calisto et al., 2008) may also result in CA 19-9 elevations. The proposed mechanism is the involvement of carbohydrate composition of CA 19-9 in inflammation and proliferation. However, Ho et al (1993) reported that normal serum CA 19-9 levels were observed in 27 patients with collagen vascular disease including systemic lupus erythematosus, scleroderma and Sjögren's syndrome. Previously, increased CA 19-9 expression was observed in patients with subacute thyroiditis especially in patients with late stage of inflammation. However, we detected no significant difference in serum CA 19-9 levels among

patients with autoimmune thyroid disease and without autoimmune thyroid diseases.

In conclusion, although the American Society of Clinical Oncology does not recommend tumor markers like CA 19-9 in screening for malignancies, they may be used for this purpose (Bast et al., 2001). In contrast to case reports showing the possible elevation of CA 19-9 in Hashimoto's thyroiditis, we did not detect such a relation. Moreover, there was no clue for the change in CA 19-9 levels in patients with hypo-, hyper- or euthyroidism.

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