Coincidence Of An Insular Thyroid Carsinoma And Chronic Lymphocytic Leukemia; A Case Report

İnsular Tiroid Karsinomu ve Kronik Lenfositk Lösemi Birlikteliği: Olgu Sunumu

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Özet

KLL olgun görünümlü eritrositlerin kan, karaciğer, kemik iliği, lenf nodları ve diğer dokularda birikimi ile karakterize hematolojik bir hastalıktır. Kronik lenfositik lösemide birlikte görülen hücresel ve humoral immün defektler nedeni ile ikincil malignıteler sık görülmekte ve enfeksiyona eğilim artmaktadır. Bu malignitelerden en sık görülenleri; büyük hücreli lenfoma (Richter Sendromu), Hodgkin hastalığı, akciğer ve cilt kanserleridir. Burada insular troid karsinomu ile kronik lenfositik löseminin nadir birlikteliği sunulmuştur.

Anahtar kelimeler: KLL, İnsülar karsinoma, İkincil malignensiler

Abstract

Chronic lymphocytic leukemia (CLL) is a hematological malignancy characterized with proliferation and accumulation of lymphocytes of mature appearance in blood, liver, bone marrow, lymph nodes and other tissues. Second malignancies occur with an increased frequency in CLL. The most frequent of these are large cell lymphoma, known as Richter's syndrome and Hodgkin's disease among hematological second malignancies, lung and skin cancers among solid tumors. The defect in humoral and cellular functions may be the underlying mechanism of increased tendency towards infections and second malignancies in CLL patients. Here we report a coexistence of insular thyroid carcinoma (ITC) and B-CLL in the same patient. The occurrence of both CLL and insular thyroid carcinoma described because of the rarity of the coexistence of these two disorders in the same patient.

Key Words: CLL, Thyroid, Insular carcinoma, Secondary malignancy

Introduction

Chronic lymphocytic leukemia (CLL) is a hematological malignancy characterized with proliferation and accumulation of lymphocytes of mature appearance in blood, liver, bone marrow, lymph nodes and other tissues. Secondary malignancies are frequent complications in patients with CLL with the standardized incidence ratio 1.59. (95% CI 1.50-1.69) (1).

Chemotherapeutic agents may also contribute to subsequent malignancies among CLL patients. Introduction of new treatment strategies including fludarabin was reported increased risk of lung cancer, acute myeloid leukemia and a more aggressive form of second malignancy (2). Alkylator-purine analog combination therapy may increase the risk of therapy-related myeloid malignancies (3). The secondary lymphoid malignancies complicating CLL includes prolymphocytic leukemia, Hodgkin disease, acute lymphoblastic leukemia, large B-cell non-Hodgkin lymphoma and multiple myeloma (4). Skin cancers, solid tumors and myeloproliferative disorders or myelodisplastic syndromes have also been documented (4-7).

The defect in humoral and cellular functions increases the tendency towards infections and secondary malignancies. Patients with chronic lymphocytic leukemia (CLL) may develop diffuse large B-cell lymphoma (DLBL), also known as Richter's syndrome. Richter's syndrome may develop in both mutated and unmutated immunoglobulin heavy-chain variable region genes of CLLs, but clonal transformation of CLL to DLBL occur only in the unmutated subgroup of CLL (8). Here we report a coexistence of an insular thyroid carcinoma and CLL.

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Case Report

A 50-year-old man referred to Ankara Numune Education and Research Hospital hematology department because of a swelling on the anterior side of his neck enlarging during the last two years. On physical examination, 15x15 cm in diameter clover sized mass which consists of combined masses on the localization of thyroid gland; multiple lympadenopathies in submandibular, inguinal and axillary region varying in size, a mass of 1x2 cm in diameter on the sixth and seventh costosternal junction and splenomegaly were detected. Laboratory values were WBC 63.200/µL, lymphocyte 58.000/µL, Hb 11.1 g/dL, and b2 micro globulin 13 mgr/L (N: 1-1, 7).

Thyroid function tests and thyroid antibodies were normal as were the platelet counts, ESR and LDH. There were mature lymphocytes and basket cells on blood smear. Bone marrow aspiration disclosed lymphocyte cell lines of 80-85 percent (Figure 3, 4). Flow cytometric analysis showed CD20 (95%), CD23 (72%), and CD19/CD5 together (40%) on lymphocytes. IgM-kappa surface immunoglobulins on B-cell lines were also detected. Findings of bone marrow examination and flow cytometry analysis were consistent with stage II CLL according to RAI Clinical Staging System. A chest tomography disclosed multiple metastatic lesions in the lungs, mediastinal lymphadenopathies and a mass on the 6^{th}, 7^{th}, and 8^{th} costae destructing the bone structure. The histopathological examination of the biopsies from the mass localized on the thyroid gland showed poorly differentiated insular carcinoma (Figure 1).

Histopathological examinations of the cervical, submandibular lymph node sections revealed the infiltrations of the tumor cells on lymph node capsule and extracapsullary field. Immunohistochemical studies showed the positive stained cells with LCA, CD-20 and lambda chain findings consistent with CLL (Figure 2). Besides, metastases of insular thyroid carcinoma on submandibular and cervical lymph nodes were seen. Thus, he underwent an operation of bilaterally thyroidectomy and debulking.

Discussion

Insular thyroid carcinoma was an interval form between well differentiated (papillary and follicular) and poorly differentiated carcinoma (anaplastic). It stems from the epithelium of thyroid follicles (9). Recently, it has been classified as a distinct entity. Thyroid insular carcinoma can develop on the ground of a goiter over in a long period. William IK et al (10) described a case of having huge goiter 2 year prior to the diagnosis of an insular thyroid carcinoma which extends through substernally. This may be inferred by proliferation, mutation, and transformatlon of the tumor physiopathology.

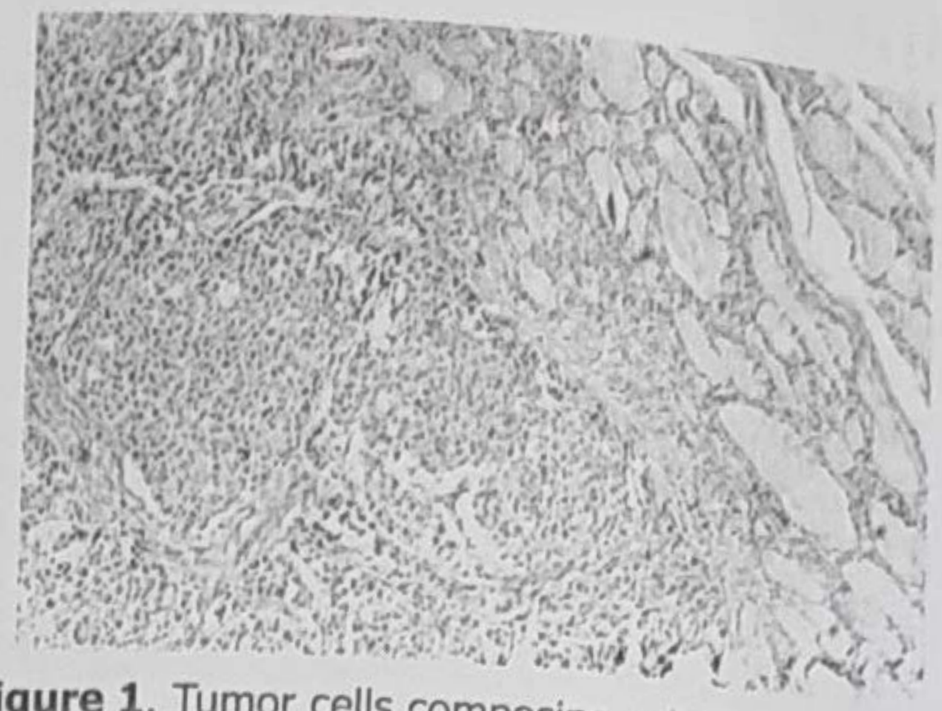

Figure 1. Tumor cells composing solid islets adjacent to thyroid tissue (X40 H&E).

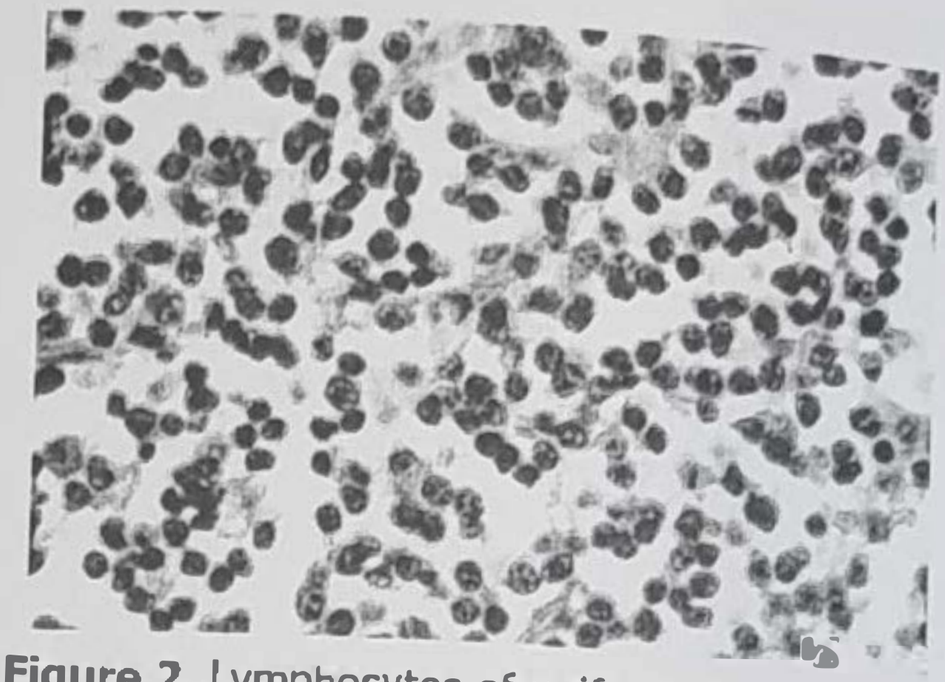

Figure 2. Lymphocytes of uniform shaped having hyperchromatic small cytoplasm in the lymph nodes adjacent to thyroid tissue (x400 H&E).

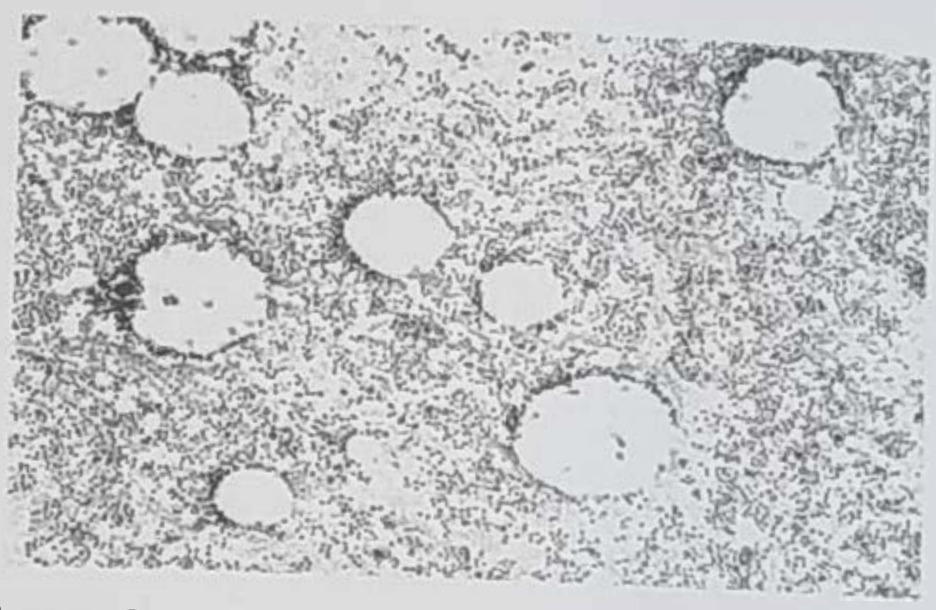

Figure 3. Lymphocytes diffusely infiltrated in bone marrow (X10, Giemsa)

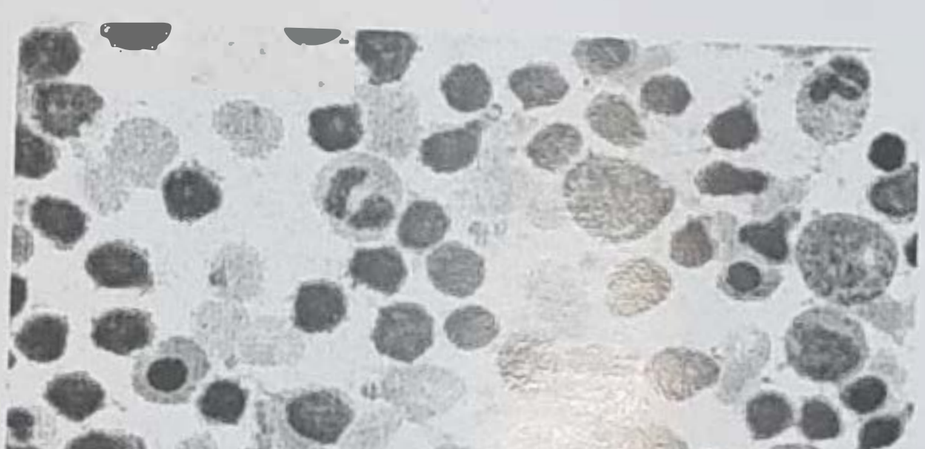

Figure 4. Lymphocytes [illegible] haped, mature appearance and hyperchrom[illegible] scanty cytoplasm in bone marrow aspi[illegible], Giemsa)

Moreover, in a 22-patient study, it is reported that 27 percent of these patients having insular thyroid carcinoma had a goiter history of 10 years or more. (11). In our case he had 25-year goiter history. There was no exposure to radiation or I-131 intake and metastasis to lungs and bones were detected. Biopsy taken from the right sixth costae revealed the metastasis of an insular thyroid carcinoma. Konturek et al. alleged to be similarities between the chromosomal changes in the thyroid carcinomas and those of the changes in breast carcinomas and CLL (12). Evarus et al. have determined dysfunction in B and T lymphocytes in early stage CLL, regulation disorder in concurrence hypothalamic–pituitary-adrenal axis, disturbance in sex hormones and changes in thyroid hormones. According to this they claimed that the disturbance in immunohormonal interactions in early-stage CLL were responsible for the pathogenesis of in this lymphoproliferative malignancy (13). Immune disturbances were accompanied by hormonal imbalance, depending on disease status: lower ACTH, cortisol and triiodothyronine levels were established to occur in active CLL compared to indolent disease (14). But, Paydas et al (15) showed an association between 7 patients previously having been diagnosed as chronic lymphoproliferative disease and thyrotoxicosis.

CLL is a classical form of human malignancy that arises from the defects of apoptosis. It occurs by the aberrations of the genes that regulate this apoptosis (16). Second malignancies in CLL occur with an increased frequency mainly result of the immune defects associated with this disease. An antigenic stimulation through the B-cell receptor is involved in the selection and possibly also the expansion of the malignant clone. Though all evidences suggest specific Ag recognition and possibly stimulation at different time-points, the nature of the Ag(s) is still unknown. It appears likely that CLL cells derive from a pool of auto/polyreactive CD5(+) B cells. (17,18).

Although among the patients having been followed with a diagnosis of CLL the risk for the development of secondary malignancies is high. No case has been reported to be diagnosed concurrently as CLL and Insular thyroid carcinoma in the literature. Likely Immunologic defects to CLL may be involved in this presentation of disease.

In conclusion, this occurrence of both CLL and insular thyroid carcinoma described because of the rarity of the coexistence of these two diseases in the same patient.

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