Primary Thyroid Lymphoma Diagnosed During Pregnancy: A Case Report

Abstract

The incidence of non-Hodgkin lymphoma (NHL) during pregnancy is quite low. There have been a few anecdotal reports of NHL arising in the thyroid gland. Here, we present a 28-year-old female patient who developed a neck swelling, pain and respiratory distress in the 17th week of her first pregnancy. She was diagnosed as having an aggressive NHL of the thyroid gland after subtotal thyroidectomy. She had 4 cycles of chemotherapy before successful cesarean delivery of a healthy, full-term male infant at 39 weeks of gestation. Four additional courses of chemotherapy were administered, after which the patient did not show any signs of relapse.

Key words: Thyroid gland, lymphoma, pregnancy, cancer

Introduction

Primary thyroid lymphoma (PTL) is a rare tumor which represents 1-5% of all thyroid malignancies, and 1-2.5% of all lymphomas (1). It is defined as a lymphoma involving only the thyroid gland or the thyroid gland and regional neck lymph nodes, without contiguous spread or distant metastases from other areas of involvement at diagnosis. Prompt recognition is important because the management of this potentially curable disease is different from the treatment of other neoplasms of the thyroid gland. Cancer is the second most common cause of death during reproductive years. It poses a very difficult challenge to the woman, her family and the doctor. The benefits of the diagnostic work-up and use of chemotherapy, radiotherapy and surgery have to be weighed carefully against their risk to the unborn baby. During pregnancy, the incidence of cancer by site include breast, melanoma, thyroid, cervix, lymphoma, and ovary in order of decreasing frequency. The vast majority of well-differentiated thyroid cancers are papillary carcinomas (2). Thyroid lymphoma is very rarely encountered during pregnancy and there are only a few case reports in the modern literature (3,4). Here, we present a case of thyroid lymphoma in a young pregnant woman and review the pertinent literature.
Case

A 28-year-old female patient complained of a large palpable swelling in the neck with associated respiratory distress of recent onset. She was in the 17th week of her first pregnancy and had no previous history or family history of thyroid disease. Physical examination revealed an enlarged thyroid gland and a body temperature of 38.5 degrees Celsius. Ultrasound of the neck showed markedly increased dimensions of the thyroid gland with a nonhomogeneous echo pattern. Her thyroid function tests were as follows: TSH: 7.43 mIU/L (0.5-4.70), FT3: 1.54 pg/mL (2.3-4.2), FT4: 0.97 ng/L (0.8-1.8). Anti-thyroglobulin antibody was positive whereas anti-thyroid peroxidase antibody was negative. Fine-needle aspiration biopsy (FNAB) from different locations within the thyroid gland was compatible with subacute thyroiditis. L-thyroxine therapy 50 µg/day was started. Because of severe respiratory distress, surgery was performed. At surgery, it was observed that the neoplasia infiltrated the loco-regional muscles and there was regional lymph node involvement as well. Subtotal thyroidectomy was performed. Microscopically, the thyroid gland was infiltrated by a diffuse proliferation of atypical, large lymphoid cells. Integrated histological and immunohistochemical analyses led to the diagnosis of diffuse large B-cell lymphoma (DLBCL) with a high proliferation index (Ki-67: 80%) and positive CD20 and BCL6 (Figure 1). Subsequent staging procedures included magnetic resonance imaging of the neck, chest, abdomen, and a bone marrow biopsy, all of which were within normal limits. The tumor was staged as IIB according to the Ann Arbor classification. Post-surgical hypothyroidism was satisfactorily managed by replacement therapy with L-thyroxine (up to 75 µg/day). Chemotherapy (cyclophosphamide, doxorubicin, vincristine and prednisone [CHOP], 8 cycles every 4 weeks) was planned and the patient underwent the first 4 cycles without vincristine. Twenty weeks after the initiation of chemotherapy she had cesarean delivery of a healthy, full-term male infant at 39 weeks of gestation. Four additional courses of chemotherapy were administered, after which the patient was reevaluated. She had no complaints and a total body computerized tomography did not show relapse of the disease.

Discussion

Thyroid lymphoma occurs primarily in middle-aged to older aged females. DLBCL is the most frequent histologic subtype of thyroid lymphomas [5]. Epidemiological evidence and indirect molecular findings from immunoglobulin heavy chain variable region gene studies suggest that chronic persistent antigen stimulation constitutes a significant pathogenetic mechanism of thyroid NHL [6, 7]. Aberrant activity of somatic hypermutation is another mechanism which may contribute to the development of lymphoid malignancies by causing genetic instability and favouring chromosomal translocation [8]. Chronic lymphocytic thyroiditis (CLT) is associated with chronic persistent antigen stimulation and present in nearly half of thyroid NHL [6-8]. Patients with PTL usually present with compressive symptoms, such as dyspnea, dysphagia and hoarseness. Positive serum antimicrosomal and thyroglobulin antibody titers were found in 68% and 34% of patients, respectively, and every patient had histologic evidence of Hashimoto’s thyroiditis in peritumor tissue [9]. Fifty-eight percent of patients were euthyroid, 14% were clinically hypothyroid, and an additional 27% had subclinical hypothyroidism [9]. Ultrasound frequently reveals a well-defined hypoecogenic mass but this feature is not unique. The diagnostic accuracy of FNAB varies widely. Because of the frequent association with CLT, the presence of lymphocytes on cytology may lead to a false diagnosis of thyroiditis and identification of lymphoma may be delayed or not possible. For these reasons, tissue biopsy (core or incisional) which enables the combination of histological stains and immunohistochemistry, is usually necessary in order to make a definitive diagnosis of thyroid lymphoma.

Thyroid lymphoma should be differentiated from lymphomas at other sites. This is especially important given the rarity of this tumor. In this case, lymphoma of the thyroid gland could be the result of secondary involvement of the gland by the tumor. Thyroid lymphoma should also be differentiated from Hashimoto’s thyroiditis and from undifferentiated or anaplastic thyroid carcinomas whose management and prognosis are totally different. In this regard, adjunctive techniques, such as immunohistochemistry and flow cytometry are particularly important. Because thyroid lymphoma is a rare disease, existing evidence for treatment is based mostly on small, retrospective studies which suffer from many severe methodological weaknesses. Therefore, optimal management remains controversial. Initially, surgery was used extensively for the treatment, but more recently chemotherapy and radiotherapy have been preferred because the

**Figure 1.** Representative images of the thyroid diffuse large B-cell lymphoma: histology (Haematoxilin-eosin), positivity for CD-20, and Ki-67 staining in patient 1 (a, b and c respectively. Original magnification×40)
tumor is chemoradiosensitive. Palliative surgery may be required to relieve compressive symptoms, especially in patients who do not respond rapidly to non-surgical treatment. On the other hand, combined chemoradiation therapy has the potential to relieve pressure symptoms without the need for an invasive intervention. When appropriately used, radiation therapy can achieve local control of the disease in a high percentage of patients (ranging from 70 up to 100%), even after long follow-up (up to 4 years) (10). Recurrence at distant sites is expected to occur in about 30% of patients and chemotherapy can control distant dissemination of the disease. Typically, patients respond rapidly to the conventional chemotherapeutic regimen CHOP (11). Combined chemoradiation therapy is associated with a significantly lower risk of distant failure. High survival rates (ranging from 75% up to 100%) have been reported following chemoradiation therapy for PTL (12).

Patients with existing thyroid diseases and cancer may become pregnant, or an initial diagnosis of thyroid cancer may be made in a patient who is pregnant. The malignancy can be well differentiated, anaplastic, or medullary. Well-differentiated thyroid cancers are frequently papillary carcinomas. Almost all well-differentiated thyroid cancers are treated by surgery and, if necessary, radioiodine and thyroid stimulating hormone suppression. Anaplastic carcinoma has a poor prognosis and is treated by external beam radiotherapy. The co-existence of thyroid lymphoma and pregnancy is a rare condition (3,4). The unusuality of this condition becomes more clear when it is considered that only approximately 100 cases of non-Hodgkin lymphoma at all sites in pregnancy have been reported so far (13,14). If diagnosed during early pregnancy, the pregnancy should be terminated and chemotherapy started immediately. In advanced pregnancy, chemotherapy should be started as early as possible. Approximately 50% of patients with non-Hodgkin disease demonstrate a complete response to therapy (14). In our patient, the decision for surgery was made because of diagnostic considerations as well as compressive symptoms and subsequent chemotherapy led to remission.

In conclusion, our case is one of the few examples of thyroid lymphoma associated with pregnancy and it was successfully managed with a combination of surgery and chemotherapy.

References