American Journal of
Experimental and Clinical Research

Am J Exp Clin Res 2020;7(1):393-395

Case Report

Sjögren syndrome complicated by acute lymphoblastic leukemia

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Abstract. Malignant lymphoma is a well-recognized occurrence in Sjögren syndrome; however, progression to acute lymphoblastic leukemia is extremely uncommon. Here we present a patient with Sjögren syndrome complicated with acute lymphoblastic leukemia. A 41-year-old male, who was diagnosed as primary Sjögren syndrome 3 months ago was admitted to our hospital due to hematuria and weakness. The complete blood count showed bicytopenia. Bone marrow biopsy and aspiration cytology confirmed the diagnosis of acute lymphoblastic leukemia. He received combination chemotherapy with prednisolone, doxorubicin, cyclophosphamide, vincristine and intrathecal methotrexate. Sjögren syndrome and other autoimmune diseases may build a portion of a continuum of lymphoproliferative disorders which have joined with B-cell neoplasms.

Keywords: Sjögren syndrome, acute lymphoblastic leukemia, malignant lymphoproliferative disorder

Introduction

Sjögren's syndrome (SS) is one of the most prevalent autoimmune disorders. Its prevalence is between 0.21% and 0.72% [1]. Cardiovascular diseases followed by malignancies and infections [2] display major reasons of death in patients with pSS. There are case reports of some malignancies including solid organ neoplasms among patients with pS [3]. Particularly, a raised risk for thyroid, lip, oral cavity, stomach, and ovarian cancer has been reported [4]. The increased occurrence of malignant lymphoma in primary pSS was first described in 1963 by Bunim and Talal [5] and then has been ascertained by others [6]. Non-Hodgkin's lymphomas (NHL) happen in about 2.7–9.8% of pSS patients and the latter data revealed that NHL risk augments 2.2% per year of age with a 4.3-fold excess risk in pSS in comparison with the other people [7]. Albeit most cells permeating the salivary glands of patients with pSS are T cells [8] the bulk of malignant lymphomas developed are of B-cell type. Here, we report one case of pSS complicated by acute lymphoblastic leukaemia (ALL).

Case presentation

A 41-year-old male, a known case of SS, visited our hospital 3 months ago with complaints of epigastric pain, frequency and hematuria which he had had for the past one week. Pain was radiating to the hypogastric area but was not associated with nausea and vomiting. The patient had experienced severe asthenia for the previous two weeks. In his past medical history there were xerostomia, xerophthalmia and swelling of the neck. That time ultrasound (US) studies had shown thyroid and bilateral submandibular gland enlargements. He was diagnosed with primary SS and was treated with oral prednisolone, hydroxychloroquine, methotrexate and oral care. At the time of new admission he looked ill and pale. A clinical examination revealed dry mouth, with no other functional signs. Sternal tenderness was obvious. Thyroid gland and both submandibular salivary glands were palpable and enlarged. There was no evidence of peripheral lymphadenopathy or hepatosplenomegaly. Blood test showed WBC =1200/ mm3, HB =13.3 g/dl,PLT= 20000/ mm3, Urea =141mg/dl, CR = 2.8 mg/dl, P= 9.1mg/dl, AST=107 IU/L, ALT=128 IU/l, LDH=3397U/L and K=4.3mEq/L. A peripheral blood smear revealed no abnormal cell. Other laboratory data were unremarkable. Chest X-rays and abdominal US were all normal. Renal US revealed normal kidney size with increased parenchychymal echogenicity but without hydronephrosis. Considering bicytopenia and after oncologist consultation, bone marrow examination was done. Histologic sections showed marrow interstitial

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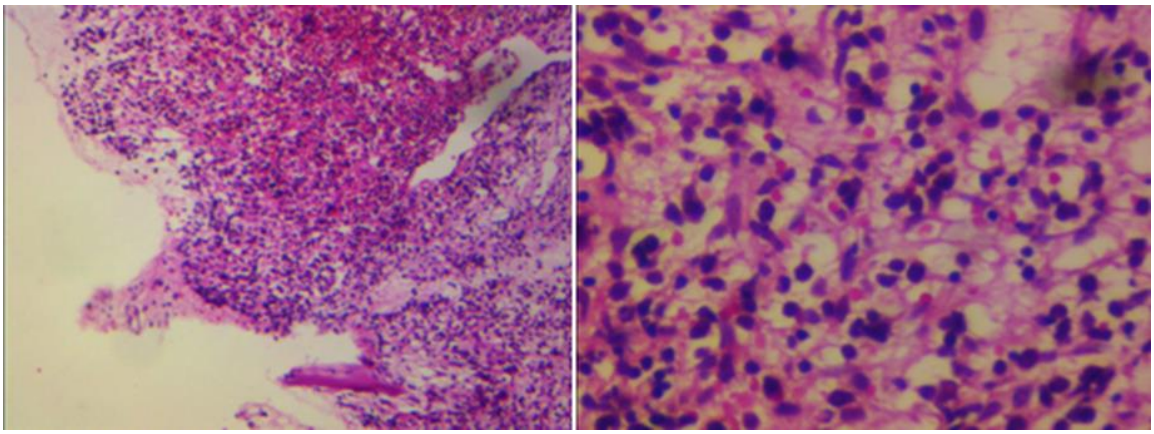

Figure 1. Histologic sections show marrow interstitial and paratrabecular infiltration by immature lymphoid cells (Hematoxylin-eosin stain; left panel x10 and right panel x40 magnification).

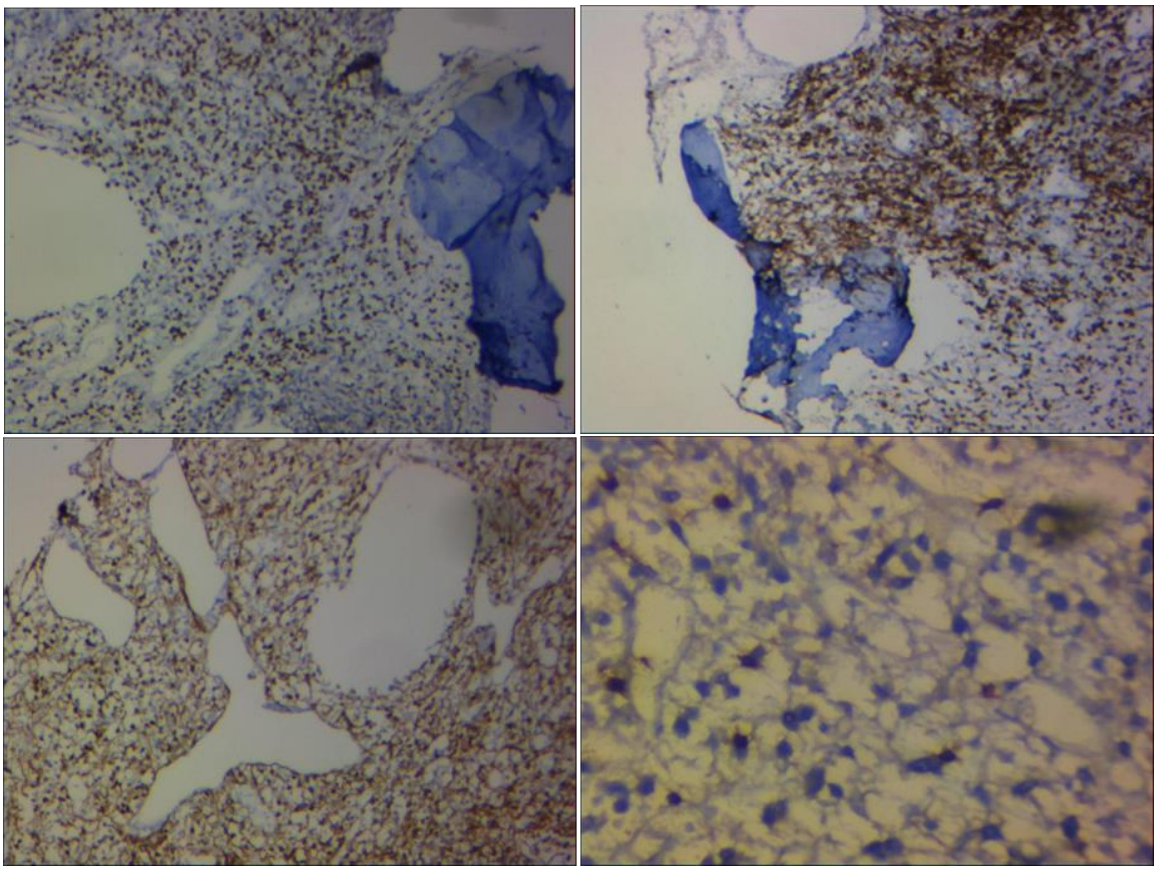

Figure 2. Neoplastic lymphoid cells were positive for TdT, CD20 and CD10 and negative for CD3 (Immunohistochemical stain; upper panels and lower left panel x10, lower right panel x40 magnification).

and paratrabecular infiltration by immature lymphoid cells (Fig. 1). IHC stains of the bone marrow revealed that neoplastic lymphoid cells were positive for TdT, CD20 and CD10 and negative for CD3 and CD 56 (Fig. 2). The patient was diagnosed with ALL (B cell type) associated with SS. Then he referred to oncology ward and received combination chemotherapy with prednisolone, doxorubicin, cyclophosphamide, vincristine and intra-thecal methotrexate. Now, the patient is in good condition after chemotherapy and is going to have a bone marrow transplant.

Discussion

The association of cancer with connective tissue diseases is well known. The oldest well-known association recorded was that of dermatomyositis with stomach adeno-carcinoma [9]. But association with other malignancies has also been reported [10]. One third of the malignancies seen in pSS are lymphomas. One research found amongst the 112 patients with pSS, 25 suffered from malignancy (before or after PSS), with malignant lymphoma developed in 11 cases. It is said that the severity of disease activity at the time of diagnosis is associated with the likelihood of

hematologic malignancies in PSS [11]. Pilar Brito-Zerón [12] got a raised risk for the development of thyroid and GI malignancies in these patients. In addition, they revealed that the patients with primary SS had an 11-fold higher risk of malignant hematological neoplasms than the general population [12]. Although there have been numerous studies [9-12] of increased risk of malignancy in patients with pSS, we have found just two cases of acute lymphoblastic leukemia in setting of pSS [11, 13]. The third published patient could be the present case. Despite these observations the cause is unknown. It is claimed that genetic changes such as mutation, amplification, deletion, chromosomal translocations and defects in DNA repair may be causative. The impact of oncogenes and certain viruses should not be overlooked [14]. On the other hand, patients with PSS are potentially subject to some degree of immunosuppression [15] therefore, these patients are rather susceptible to secondary malignancies such as hematologic neoplasms. The use of disease-modifying medication in autoimmune diseases may be associated with an increased risk of malignancy. Due to factors not well known. It is probable that polyclonal B cell proliferation may be transformed to monoclonal ones and finally transform to malignant lymphoproliferative disease. However, this possibility should be interpreted with caution as the use of these drugs is limited to cases with severe illness. Lazarus et al. did not find any significant differences in the use of immunomodulatory drugs consumed to treat severe forms of SS when comparing these patients with or without malignancy [11]. The question that arises here is whether or not Sjögren syndrome is a paraneoplastic syndrome in our patient? Short gap between onset of pSS symptoms and lymphoblastic leukemia is in favor of paraneoplastic syndrome. Another study suggested the possible paraneoplastic nature of SS [16]. It is likely that SS and other autoimmune diseases build portion of a continuum of lymph proliferative disorders which have joint genesis with B-cell neoplasms. In this regard, development of acute lymphoblastic leukemia may be the result of genesis of an eternal clone. However, the concordance of these two diseases is indicative of a possible causal relation.

Conclusion

Patients with pSS should be closely monitored for the possibility of hematologic and solid malignancies.

Conflict of Interest

The authors declare no conflicts of interest.

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