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An Intriguing Combination: Sjogren Syndrome Coexisting with Hodgkin Lymphoma

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Abstract

While Hodgkin's lymphoma is a lymphoid malignancy, Sjögren's syndrome is an autoimmune disorder marked by exocrine gland inflammation. Sjögren's syndrome (SS) is a chronic autoimmune condition marked by lymphocytic infiltration of the exocrine glands, primarily the salivary and lachrymal glands, which typically manifests as xerostomia and xerophthalmia. Lymphoma is the most dreaded of these systemic sequelae, which are present in about 50% of individuals with primary SS. These neoplasias are mostly non-Hodgkin and arise from B cells. It is unusual for these two diseases to coexist, and the underlying mechanisms are not entirely understood. Viral infections, genetic components, and persistent antigenic stimulation are a few hypotheses that have been proposed. In patients with Sjögren's syndrome, Hodgkin's disease can present with a variety of clinical characteristics, including as lymphadenopathy, B symptoms, extranodal involvement, and immunological abnormalities. The impact of therapy on the symptoms of Sjögren's syndrome necessitates a multidisciplinary approach to treatment. The relationship between these two conditions must be established, and additional research is required to offer potential reasons. Due to the possibility of relapse or the emergence of new malignancies, long-term follow-up is crucial. We discuss the case of a 17-year-old girl who was diagnosed with Hodgkin's lymphoma and primary Sjögren's disease.

Keywords: Hodgkin Lymphoma, Sjögren's Syndrome, Autoimmune Disease, Lymphoma Development, Chronic Antigenic Stimulation, Extra Nodal Involvement, Immunological Abnormalities

Introduction

Sjogren syndrome (SS) is a frequent kind of systemic autoimmune illness that is typically restricted to the exocrine glands (mostly the salivary and lachrymal), which causes the desiccation of oral and ocular mucosal tissues. But some people with SS may experience systemic symptoms, and B-cell non-Hodgkin lymphoma (NHL) development is a serious consequence that affects about 5% of patients [1]. The heightened risk of development of non-Hodgkin's lymphoma as a complication in patients with sjogren syndrome is well documented [2, 3]. Most of the lymphomas are derived from B cells. However T cell lymphomas have also been reported with primary and secondary sjogren syndrome [4].

The risk of non-Hodgkin lymphoma (NHL) among systemic autoimmune illnesses is highest in Sjögren's syndrome (SS), where it is estimated to be 7 to 19 times greater than in the general population. In SS patients, this elevated risk is a serious concern. The mucosa-associated lymphoid tissue (MALT) lymphoma, which is mainly seen in the salivary glands, is the most common histological lymphoma type in primary SS patients. A primary SS patient's likelihood of developing this type of lymphoma is astonishingly high—it is about 1000 times higher. It's crucial to keep in mind, though, that more aggressive subtypes, such diffuse large B-cell lymphomas, can also manifest in this situation. It can be difficult to distinguish lymphoma from benign gland enlargement, however methods like MRI and ultrasonography with Doppler can be useful. The histological subtypes MZL (marginal zone lymphoma) and DLBCL (diffuse large B-cell lymphoma) are both common [5, 6, 11].

The coexistence of Hodgkin's disease and primary Sjogren's syndrome is rare. Possible explanations include chronic antigenic stimulation, genetic factors, and viral infections such as Epstein-Barr virus. Further research is needed to understand the underlying mechanisms [7]. Lymphomagenesis is thought to be a complex and multifaceted process that is still not fully understood in the setting of autoimmunity, notably in Sjögren's syndrome (SS). Genetic abnormalities such chromosomal translocations, mutations of the tumor suppressor gene p53, and polymorphisms of molecules involved in immune activation pathways are only a few of the causes that have been suggested. The development of non-Hodgkin lymphoma (NHL) associated with SS has also been linked to specific clinical characteristics at the time of disease presentation. These characteristics include visible purpura, persistent salivary gland enlargement (SGE), lymphopenia, monoclonal type II cryoglobulinemia, and hypocomplementinemia in the laboratory. Also linked to a higher risk of NHL in SS patients are significant lymphocyte infiltrations and germinal center development in small salivary gland biopsies [8, 9, 10, 11].

Based on these results, SS patients can be divided into several subsets with different chances of getting lymphoma, which can be evaluated at the time of their initial assessment.

We present a case of a 17-year-old girl, diagnosed with Hodgkin's lymphoma since 6 months, presented with hypokalemic paralysis and labaratory evidence of distill renal tubular acidosis. She had a history of dry eyes, dry mouth and itching of eyes since 6 years. Autoimmune profile and clinical test confirmed sjogren syndrome. This case highlights the association of Hodgkin's lymphoma and sjogren syndrome which has rarely been reported. Further studies need to be conducted to establish this association and offer its possible explanation.

Case Report

A 16-year-old girl who has had Hodgkin lymphoma for the previous six months was diagnosed with the disease and came with several episodes of watery, non-projectile vomiting and loose watery feces. She also reported having generalized, cramping stomach pain the previous day. She started to feel weak in all four limbs the next day. Her legs were first affected by this gradual, developing weakness, which later expanded to her arms over the course of the following several hours.

She had experienced sporadic fevers throughout the previous six months. The high-grade fever, which peaked at 102°F, occurred every eighth day and lasted for three days at a time. It had nothing to do with rigors, chills, or perspiration. Additionally, the patient mentioned a major weight loss of 6 kg in a month as well as generalized bodily weakness.

She had an ANA profile performed before to arriving at our medical emergency department, and the results revealed a speckled pattern. She had a 25.3 IU/ml RA factor. A bone marrow biopsy revealed that Hodgkin lymphoma with a CD3-reactive pattern was more likely to infiltrate the bone marrow. Her face, neck, chest, belly, and pelvis were all shown to have cervical and axillary lymphadenopathy by a CT scan. Good biventricular systolic function was seen on transthoracic echocardiography.

For the preceding two months, the patient had been undergoing chemotherapy for Hodgkin lymphoma with Adriamycin, Bleomycin, Vinblastine, and Dacarbazine. She had finished 4 sessions altogether, one every 15 days.

Her vital signs at presentation were as follows: 99 beats per minute for heartbeat, 90 beats per minute for blood pressure, 100 beats per minute for respiratory rate, 169 beats per minute for blood sugar, and 99% for room air saturation for SpO2.

The patient had a GCS of 15/15, seemed dehydrated and pale, and all of his cranial nerves were intact. She displayed a vaguely defined flaccid quadriparesis while maintaining control over her urination and feces. Babinski's response was bilateral flexor contraction.

Characteristics	Right Upper limb	Left Upper limb	Right Lower limb	Left Lower limb
Bulk	Reduced	Reduced	Reduced	Reduced
Tone	Normal	Normal	Normal	Normal
Power	1/5	1/5	1/5	1/5
Reflexes	Diminished	Diminished	Diminished	Diminished

Other systemic analysis was unremarkable.

Initial lab testing uncovered: Haemoglobin: 8.8 gm/dl, TLC: 1.64x10^3 / uL, Platelets: 119 x 10^3 / uL, Lymphocytes: 12%, Neutrophils: 58%, Albumin: 3.7g/dl, Calcium: 8.8 mg/dl, Sodium: 142 mmol/L, Potassium: 1.5 mmol/L, Chloride: 116mmol/L, Magnesium: 2.0 mg/dl, Serum Bicarbonate: 16 mmol/L, Urea: 41 mg/dl, Serum Creatinine: 1.17 mg/dl, Total Bilirubin: 0.33mg/dl, ALP: 97 U/L, AST: 52 U/L, ALT: 15 U/L, PT: 14 seconds, aPTT: 35 seconds. The ABGs revealed a pH of 7.374, pCO2 of 20.0 mmHg, and pO2 of 90 mmHg.

The patient was initially given potassium replacement therapy for hypokalemic periodic paralysis. Her vomiting and diarrhea stopped, and all of her limbs' muscle strength increased to 5/5. Her serum potassium levels continued to be chronically low despite potassium replenishment. Magnesium levels in the blood were normal. A few days after the diarrhea stopped, a venous blood gas revealed a normal anion gap metabolic acidosis (anion gap equal to 9), which raised the likelihood that renal tubular acidosis was the cause of the patient's hypokalemia. Spot urine potassium was 45 mmol/l.

Her urine complete examination showed pH of 6.0, specific gravity: 1.030 with trace proteins and 3-5 RBCs and 3-5 epithelial cells/HPF. To work up for the cause of renal tubular acidosis, her detailed history was sought again where she recalled that she had been having dry eyes that would itch a lot, dry mouth with difficulty in swallowing and vaginal dryness for last 7 years. Subsequently, the ENA profile revealed positive antibodies related to Sjögren's syndrome. Anti-SSA/Ro 60kD: 100 U/ml, Anti-SSA/Ro 52kD : 99 U/ml and Anti-SSB/La : 78 U/ml in the presence of sicca symptoms, a presumed diagnosis of Sjögren's syndrome was made which was further supported by Schirmer's test.

Results of serological investigations

ANA	Speckled pattern
RA factor	Positive
Anti-SSA	Positive
Anti-SSB	Positive
Anti-smith	Negative
Anti-RNP	Negative
Anti-Jo1	Negative
Anti Scl-70	Negative
Anti ds-DNA	Negative

Discusson

Sjogren's syndrome is an chronic inflammatory autoimmune process characterized by lymphocytic infiltration of exocrine glands together with polyclonal B cell activation, as illustrated by the presence of multiple circulating autoantibodies against organ- and nonorgan-specific autoantigens [12]. Histologically, Sjogren's syndrome is characterized by mononuclear cellular infiltration of the salivary and lacrimal glands, while serologically, it is characterized by the presence of many tissue component antibodies [16].

Since Talal's study in 1964, a number of researchers have emphasized the link between Siogren's disease and the emergence of malignant lymphoma. Both in the typical case of B cell lymphomas5 and in the uncommon cases with T cell lymphoma, it has been proposed that this connection may be caused by a prolonged state of immunological hyperactivity [2].

Depending on the stage and severity of the disease, clinical features can change in people with primary Sjogren's syndrome and Hodgkin's disease. Common characteristics include lymphadenopathy, B symptoms like fever, night sweats, and weight loss, extranodal involvement, particularly in the salivary and lacrimal glands, histological findings that are consistent with both conditions, immunological abnormalities, and treatment considerations that call for a multidisciplinary approach. These elements make treating Hodgkin's disease in those with primary Sjogren's syndrome more difficult [16, 17]. The clinical spectrum ranges from exocrine gland dysfunction to multisystem disorder involving musculoskeletal, renal, vascular and gastrointestinal tract. Renal tubular acidosis is commonly associated with sjogren syndrome and often presents with persistent hypokalemia [20].

Patients with sjogren syndrome have a greater tendency to develop lymphoid malignancies. The primary step in transition of autommune process to malignancy involves conversion of polyclonal to monoclonal activation of B cells [13]. Many case reports have documented the association of NHL with sjogren syndrome. The prevalence of NHL in sjogren syndrome is 4.3%, the most common being marginal-zone B cell lymphoma [3, 14, 15].

Standard treatment regimens for Hodgkin lymphoma are followed in the management of Hodgkin's disease in primary Sjogren's syndrome. Bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, and prednisone are major chemotherapy agents used in ABVD or BEACOPP regimens, respectively. When treating localized disease or consolidating treatment after chemotherapy, radiation therapy may be explored [19].

Hodgkins lymphoma in patients with primary sjogren syndrome has rarely been reported [16, 18]. Our patient, biopsy proven case of Hodgkins lymphoma, had features suggestive of sjogren syndrome that started years before lymphoma but remained undiagnosed. Our diagnostic approach of this patient deserves some comment. The patient was diagnosed after testing positive for anti Ro/LA antibodies along with schirmer test (focus score of 4). However, we could not perform labial gland biopsy as it was not consented by the patient. Furthermore, as sjogren was diagnosed in retrospect after suggestive symptoms preceeding lymphoma, we could not be sure of when exactly she developed primary sjogren syndrome and the time interval between sjogren syndrome and Hodgkin's lymphoma.

The cause of Hodgkins disease in patients with sjogren is still unknown. We advocate further studies to develop association between sjogren and Hodgkins lymphoma and offer some possible explanation. These patients should be monitored for development of lymphoma as complication. In addition, hypokalemic periodic paralysis can be a presentation of renal tubular acidosis, therefore; it should be suspected in patients presenting with persistent hypokalemia.

The prognosis in these instances is typically good, with outcomes resembling Hodgkin's disease without Sjogren's syndrome. The risk of disease recurrence or the emergence of other cancers, however, makes long-term follow-up imperative. This case highlights the need for more research in this area. There is a necessity for researchers to investigate this subject and offer insightful findings to the medical community because there is little existing literature on this particular presentation. We can better comprehend the underlying mechanisms, diagnostic approaches, and therapy options for patients with comparable presentations by carrying out rigorous investigations and broadening our knowledge base. To better understand this uncommon ailment and provide better patient care, collaboration between researchers, doctors, and specialists in relevant fields is essential.

Conclusion

Hodgkin lymphoma is a lymphoid cancer, whereas SS is an autoimmune illness marked by gland inflammation. Non-Hodgkin lymphoma risk is higher in SS patients, however the connection between SS and lymphoma development is not entirely understood. Although diagnosis might be difficult, imaging techniques can help to separate cancer from benign gland enlargement. For Hodgkin lymphoma, conventional protocols are used for treatment. To further understand the connection between SS and Hodgkin lymphoma and direct clinical care, more research is required.

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