Case Report

Bilateral Lacrimal Gland Lymphoma in Sjögren Syndrome

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1. Introduction
Sjögren syndrome is a chronic autoimmune condition which goes along with lymphocytic and plasma cell infiltration of the salivary and lacrimal glands progressively. This gland infiltration finally leads to xerostomia and keratoconjunctivitis sicca [1]. Sjögren syndrome might be either primary or accompanying other autoimmune diseases [1]. It is well known that, in patients with Sjögren syndrome, lymphoproliferative activity, benign to malign, is significantly increased [2, 3]. In Sjögren syndrome the relative risk of lymphoma is estimated to be 16–18 times higher than the normal population [4, 5]. Herein we report bilateral lacrimal gland lymphoma in a female with Primary Sjögren Syndrome (pSS).

2. Case Presentation
A 31-year-old female with pSS for 3.5 years experiencing bilateral periorbital puffiness for 3 years was evaluated. Upon inspection lacrimal gland regions were bilateral puffy (Figure 1(a)). Eversion of the eyelids led the view of hypertrophic and edematous bilateral lacrimal glands. Best corrected visual acuity was 20/20 in both eyes with normal anterior and posterior segment evaluation. Schirmer 1 score was 2 and 1 mm and tear-film break-up time was 3 and 4 seconds, in the right and the left eyes, respectively. An incisional biopsy from the left lacrimal gland revealed diffuse and intense CD20, CD5, and bcl-2 positivity with negative cyclin D1 and CD23 (Figures 2(a)–2(f)). The results supported lymphoma; however, the exact histological discrimination could not be made. The patient was consulted to haematology department and as lacrimal gland was affected extranodal marginal zone lymphoma diagnosis was made. CHOP (cyclophosphamide, doxorubicin, vincristine, and methyl prednisolone) treatment was initiated. In conclusion, pSS is a well known autoimmune disease in which increased rate of lymphoma is present. Early detection with histopathologic confirmation and multidisciplinary approach with ophthalmology, rheumatology, and haematology are mandatory in these patients.
3. Discussion

The diagnosis of lymphoma in Sjögren syndrome is well documented and lymphoma is recognized as the most important complication in the disease progress [4]. The evolution from the lymphoepithelial disease to lymphoma is likely to be a multiphase activity [6]. Lymphoepithelial disease is mostly seen as a compound of polyclonal B and T cells, whereas lymphoma shows neoplastic monoclonal B-cell proliferation [3]. An intermediate stage lymphoproliferative activity in the spectrum of benign to malignant lymphocytic proliferation is accepted as pseudolymphoma [5].

In patients with Sjögren syndrome various histologic subtypes of lymphoma, most of which are low-grade B-cell malignancies, have been described [7]. It is reported that mucosa associated lymphoid tissue lymphoma constitutes 46 to 56% of the lymphomas, developing in Sjögren syndrome patients [7].

The higher risk of developing lymphoma in Sjögren’s syndrome is predicted to increase with time of the diagnosis. However, the risk is reported not to be related to the patient age at pSS diagnosis and is reported to be less among patients without any bad predictive factors [5]. It is advised that whenever asymmetrical enlargement of parotid or lacrimal glands, palpable masses in the glands, refractory lymphadenopathy, and splenomegaly are detected, lymphoma should be suspected and investigated. Herein, the diagnosis time of pSS was 3.5 years earlier and bilateral puffiness around lacrimal gland region was experienced for 3 years. What makes this case unique is the bilateral lymphoma involvement of the lacrimal glands in pSS, to our knowledge the first one in the literature.

Treatment options for marginal zone lymphoma (MZL) are considered when patients have limited stage, advanced stage, and location of disease. Although patients with limited stage MZL are managed with radiotherapy (24–36 Gy), rituximab monotherapy and rituximab combined with chemotherapy need to be evaluated. Rituximab-CHOP combination therapy is the standard treatment option in advanced stages [8, 9]. As the reimbursement agency does not pay for rituximab in this clinical state, we treated the patient with only CHOP regimen.
In conclusion, rate of lymphoma in patients with pSS is markedly increased. For this reason, imaging techniques especially focusing on the head and neck regions including the lacrimal glands are sine qua non in the follow-up of pSS patients. Any enlargement of the lacrimal glands even if bilateral should be investigated for possible lymphoproliferative disease.

Disclosure

This case was presented in ESCRIS 2015 Barcelona, Spain, as a poster.

Competing Interests

The authors declare that they have no competing interests.

References

[1] R. I. Fox, F. V. Howell, R. C. Bone, and P. E. Michelson, "Primary sjogren syndrome: clinical and immunopathologic features," *Seminars in Arthritis and Rheumatism*, vol. 14, no. 2, pp. 77–105, 1984.

[2] N. A. Cummings, G. L. Schall, R. Asofsky et al., "Sjögren's syndrome: newer aspects of research diagnosis and therapy," *Annals of Internal Medicine*, vol. 75, pp. 937–950, 1971.

[3] H. Tonami, M. Matoba, Y. Kuginuki et al., "Clinical and imaging findings of lymphoma in patients with Sjögren syndrome," *Journal of Computer Assisted Tomography*, vol. 27, no. 4, pp. 517–524, 2003.

[4] E. Theander, G. Henriksson, O. Ljungberg, T. Mandl, R. Manthorpe, and L. T. H. Jacobsson, "Lymphoma and other malignancies in primary Sjögren's syndrome: a cohort study on cancer incidence and lymphoma predictors," *Annals of the Rheumatic Diseases*, vol. 65, no. 6, pp. 796–803, 2006.

[5] R. Solans-Laquè, A. López-Hernandez, J. Angel Bosch-Gil, A. Palacios, M. Campillo, and M. Vilardell-Tarres, "Risk, predictors, and clinical characteristics of lymphoma development in primary Sjögren's syndrome," *Seminars in Arthritis and Rheumatism*, vol. 41, no. 3, pp. 415–423, 2011.

[6] N. Sutcliffe, M. Inanc, P. Speight, and D. Isenberg, "Predictors of lymphoma development in primary Sjögren's syndrome," *Seminars in Arthritis and Rheumatism*, vol. 28, no. 2, pp. 80–87, 1998.

[7] M. Voulgarelis, U. G. Dafni, D. A. Isenberg, and H. M. Moutsopoulos, "Malignant lymphoma in primary Sjögren's syndrome: a multicenter, retrospective, clinical study by the European concerted action on Sjögren's syndrome," *Arthritis and Rheumatism*, vol. 42, no. 8, pp. 1765–1772, 1999.

[8] J. S. Goda, M. Gospodarowicz, M. Fintilie et al., "Long-term outcome in localized extranodal mucosa-associated lymphoid tissue lymphomas treated with radiotherapy," *Cancer*, vol. 116, no. 16, pp. 3815–3824, 2010.

[9] B. Kahl and D. Yang, "Marginal zone lymphomas: management of nodal, splenic, and MALT NHL," *Hematology/The Education Program of the American Society of Hematology*, vol. 2008, no. 1, pp. 359–364, 2008.