A case of Sjögren's syndrome presenting with conjunctival lymphoma

Sirs,

Sjögren's syndrome (SjS) is a systemic autoimmune disease characterised by chronic inflammation of the exocrine glands, and by a rather frequent occurrence of B cell lymphoma, namely mucosal-associated lymphoid tissue (MALT) lymphomas (1). Conjunctival MALT lymphomas are a rare, low-grade type of non-Hodgkin lymphoma (NHL) that may affect the eye (2). We present here an intriguing case of a woman who was diagnosed with SjS shortly after the development of a conjunctival lymphoma.

A 52-year-old woman referred in October 2022 to an ophthalmologist complaining of an acute foreign body sensation in her right eye; pulling her inferior eyelid, she could appreciate a crescent-shaped, 1 cm length chemosis of the conjunctiva.

A conjunctival specimen, obtained from a local biopsy, showed focal subepithelial aggregates of $CD138^+$ atypical plasma cells, expressing monoclonal g light chains. Small lymphocytes were also present, mainly $CD20^+MNDA^+$ B lymphocytes, and a minority of $CD3^+CD5^+$ T cells. Mib-1 proliferation index was 2%. Submucosal perivascular deposits of amyloid were observed as well (Fig. 1). Therefore, a diagnosis of conjunctival MALT lymphoma with marked secretory differentiation was made. The patient denied weight loss, nocturnal sweats, or malaise. No superficial lymph node, liver and spleen enlargement was observed, nor orbital or cerebral lesions on magnetic resonance imaging (MRI). Histology and immunofluorescence on bone marrow biopsy excluded lymphomatous infiltrates.

After local radiotherapy, the patient achieved complete response.

In August 2023, a second MRI of the head showed reduced size of her parotid and submandibular glands with "salt and pepper" pattern, raising suspicion for SjS. However, she did not complain of sicca symptoms until February 2024, when she developed symmetric swelling of the second and third proximal interphalangeal joints of both hands and dry mouth feeling. Serological tests showed high titre positivity of antinuclear antibodies (ANA), anti-Ro-52kD and -60kD and anti-La antibodies and mild reduction of C4 complement fraction. Schirmer's test was positive also in non-radiated eye (<5 mm in 5 minutes). According to the 2016 ACR/EULAR classification criteria (3), a diagnosis of SjS was established. The patient was started on hydroxychloroquine and low-dose corticosteroids. After two months, the patient reported feeling better, allowing her corticosteroid dose to be tapered down.

Conjunctival lymphoma has a worldwide incidence of 0.2 per 100,000 and accounts for 1-2% of all NHLs (2). Its clinical onset may simulate that of a SjS for the frequent presence of dry eyes.

SjS is a recognised risk factor for the development of lymphomas, the relative risk being ascertained to be 13.71 (95% CI 8.83, 21.29) (4). Consequently, a careful monitoring is required during the follow up of patients with SjS. Only few cases have been previously reported of conjunctival MALT lymphoma developing during SjS (5-7). To our knowledge, this is the first reported case in which the patient developed a SjS after the diagnosis of a conjunctival lymphoma.

The relationship between lymphoma and SjS has been defined as bidirectional since in large epidemiological survey it has been shown that among 25,074 Taiwanese patients with NHL, 49 developed SjS after the diagnosis of lymphoma (8). It is well known that in SjS, as in other autoimmune diseases, specific serum autoantibodies can be found many years before symptoms onset (9) These specific autoantibodies (*i.e.*, ANA, anti-Ro and -La antibodies) are capable to induce a persistent stimulation of B cells by linking BCR, TLR9 and a particular CDR3 (this latter predominantly expressed on MALT lymphoma cells from salivary glands) (10).

This case report highlights again that a screening for such autoantibodies in patients with B cell, namely MALT, lymphomas may be useful to predict the following development of SjS.

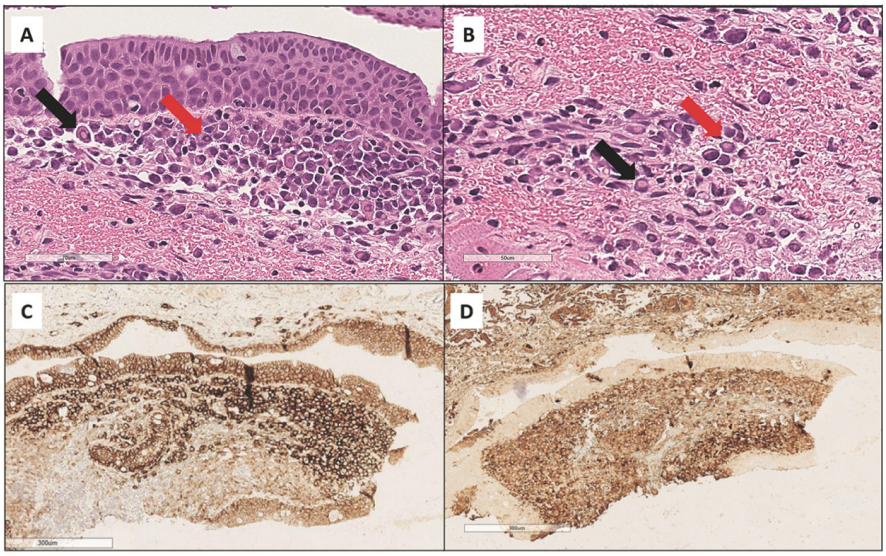

Fig. 1. Bioptic sections of lymphomatous lesion showing small aggregates of lymphoid cells and plasma cells, the latter presenting evident nuclear (Dutcher bodies, red arrows) and cytoplasmic (Russel bodies, black arrows) inclusions (**A-B**). Immunohistochemical reactions for CD138 stains the plasma cells infiltrate (**C**) with mono-typical expression of λ light chains (**D**).

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