

1. **Q:** Schirmer's test, what value did you collect unstimulated whole saliva. If so, what value.

A: According to the 2016 ACR/EULAR classification criteria for SS, Schirmer's test result ≤ 5 mm/5 min in at least one eye and unstimulated whole saliva flow rate flow rate ≤ 0.1 mL/min are regarded as positive (having a weight of 1 each). Schirmer's test results were 5 mm /10 min in left eye and 14 mm/10 min in right eye of our patient, and the results were positive. Unstimulated whole saliva flow rate flow rate of our patient was 1.5ml/10min, which was negative.

2. **Q:** Was the diagnosis solely based on the positive biopsy and abnormal Schirmer.

A: First, the patient met the inclusion criteria (with symptom of oral dryness for more than 3 months), and didn't have any of the conditions as exclusion criteria (history of head and neck radiation treatment, active hepatitis C infection, AIDS, sarcoidosis, amyloidosis, graft-versus-host disease, IgG4-related disease), and then was diagnosed as SS with positive labial salivary gland biopsy(focus score of \geq foci/4 mm²) and abnormal Schirmer's test (≤ 5 mm/5min in at least one eyes) according to the 2016 ACR-EULAR classification criteria for SS.

3. **Q:** The typical signs of a MALT lymphoma were not present (swelling of the glands, low c3/c4, hypergammaglobulinemia, cryoglobulinemia), explain why these signs were not present.

A: A subsequent retrospective study investigated hematologic manifestations and predictors of lymphoma in 536 SS patients (40 with lymphoma)^[1]. Among 5 risk factors identified by multivariate analysis as predictors (cryoglobulinemia, low C4 levels, neutropenia, splenomegaly and lymphadenopathy) the proportion of SS patients developing lymphoma by number of risk factors was 3.62%, 11.96%, 34.78%, 80% and 100% in patients with 0, 1, 2, 3, and 4 risk factors, respectively. That means SS patients without these "old predictors" may also develop lymphoma. Further prospective studies are required. Besides, this may have been because the MALT lymphoma involved skin rather than the parotid gland in our case, and the

typical signs of a MALT lymphoma were not present (swelling of the glands, low c4, cryoglobulineamia).

4. **Q:** Also the patient is not a typical SS patient. How could all patients fulfil the ACR/EULAR criteria, retrospectively?

A: Classified according to the ACR/EULAR criteria, our patient was diagnosed with SS when admitting to our department, prospectively.

5. **Q:** 1000 fold increase of lymphoma in SS patients? Is that not too high?

A: In the study conducted by Ekström Smedby et al^[2], among the 40 SS patients with NHL of known anatomic site, 10 were MALT lymphomas situated in the parotid gland, corresponding to a 1000-fold risk of parotid gland MALT lymphoma (OR=996; 95% CI, 216-4596). This finding is consistent with prior SS lymphoma case series^[3], and with biologic evidence of antigen-driven clonal expansions in affected salivary glands^[4].

6. **Q:** Why did you not include the larger series in your table?

A: According to the searching result, 87 articles were identified and 26 articles fulfill our inclusion criteria. But it is regrettable that the largest case series only include 4 cases.

REFERENCES

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- 2 **Ekström Smedby K**, Vajdic C, Falster M, Engels E, Martínez-Maza O, Turner J, Hjalgrim H, Vineis P, Seniori Costantini A, Bracci P, Holly E, Willett E, Spinelli J, La Vecchia C, Zheng T, Becker N, De Sanjosé S, Chiu B, Dal Maso L, Cocco P, Maynadié M, Foretova L, Staines A, Brennan P, Davis S, Severson R, Cerhan J, Breen E, Birmann B, Grulich A, Cozen W. Autoimmune disorders and risk of non-Hodgkin lymphoma subtypes: a pooled analysis within the InterLymph Consortium.*Blood* 2008; **111**:

- 4029-4038 [PMID:18263783 doi: 10.1182/blood-2007-10-119974]
- 3 **Voulgarelis M**, Dafni U, Isenberg D, Moutsopoulos H. Malignant lymphoma in primary Sjögren's syndrome: a multicenter, retrospective, clinical study by the European Concerted Action on Sjögren's Syndrome. *Arthritis and rheumatism* 1999; **42**: 1765-1772 [PMID:10446879 doi: 10.1002/1529-0131(199908)42:8<1765::aid-anr28>3.0.co;2-v]
- 4 **Yamamoto K**. Pathogenesis of Sjögren's syndrome. *Autoimmunity reviews* 2003; **2**: 13-18 [PMID:12848970 doi: 10.1016/s1568-9972(02)00121-0]