

## Letters to the Editor

### Infliximab therapy in patients with secondary Sjögren's syndrome: Functional evaluation

Sirs,

Sjögren's syndrome (SS) is a chronic inflammatory disease characterised by a decrease in lacrimal and salivary secretion also called autoimmune epithelitis. The prevalence of SS is relatively high: for the primary disease it is 1/2500, while secondary Sjögren's syndrome may be found in up to 30% of patients with systemic lupus erythematosus (SLE) and in up to 20% in patients with rheumatoid arthritis (RA) (1).

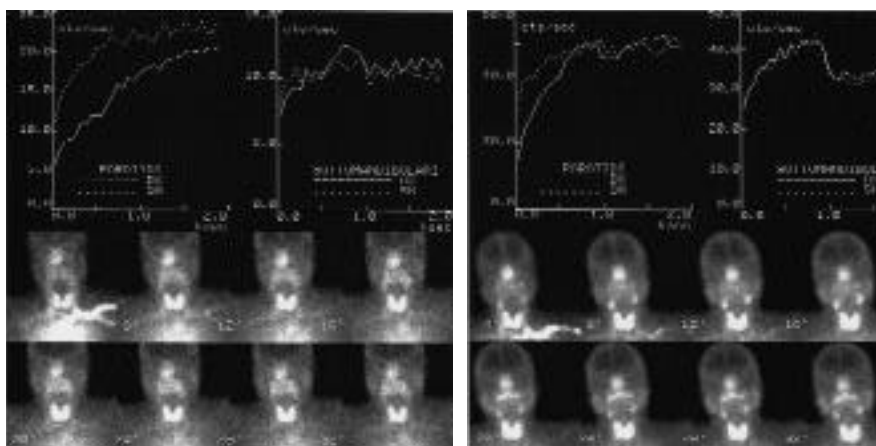
It would be useful to find a therapeutic agent that inhibits the inflammatory process in the salivary glands and prevents further destruction of residual function. The therapeutic options available so far, however, such as immunosuppressive agents or corticosteroids, are limited, not highly effective and characterised by several undesirable side effects (2). Treatment is most often aimed at increasing saliva production by means of sialagogous drugs.

TNF- $\alpha$  plays a central role in the pathogenesis of inflammatory processes; it modulates the secretion of cytokines such as IL-8, and upregulates the expression of adhesion molecules (ICAM) on endothelial cells and of integrins on granulocytes with a consequent increase in the recruitment of polymorphonuclear cells at the sites of inflammation (3).

Steinfeld *et al.* have recently showed that infliximab may be useful for the treatment of SS (4). Studies performed so far, however, have not evaluated the effect of therapy on the function of infiltrated glands. We report our experience with the use of infliximab (Remicade®) in 4 female patients with RA and secondary SS (mean age: 49, range: 34-60 years) diagnosed according to the criteria of the American Rheumatology Association (ARA). The following parameters were evaluated: complete blood cell count, renal and liver function tests, ESR, CRP, ANA, ENA, anti-dsDNA antibodies and ophthalmologic assessment with Schirmer's test and tear film break-up time (BUT). At the time of the study all patients were being treated with methotrexate or cyclosporin A and were showing disease progression. Written informed consent was obtained from all patients.

Infliximab was given according to the protocol used in the ATTRACT study: 3 mg/kg in infusion at the following time points: 0, 2, 6, 14, 22 and 30 weeks in combination with methotrexate or cyclosporin A.

To evaluate the effect of therapy on the function of salivary glands, scintigraphy was performed immediately before the be-



**Fig. 1.** Salivary gland scintigraphy in a patient with rheumatoid arthritis and secondary Sjögren's syndrome before (A) and after (B) treatment with infliximab. The uptake curves (DX: right, S:left) of the baseline study show decreased and delayed uptake and no significant response to lemon juice. The images show severe reduction of pertechnetate uptake in the all major salivary glands, comparable to background activity. The study after therapy shows, both in the curves and in the images, increase in tracer uptake and the appearance of a response to lemon juice in all major salivary glands, being particularly evident in the submandibular glands.

ginning of treatment and was repeated after 3 months. Dynamic images were acquired after the injection of 185 MBq of  $^{99m}\text{TcO}_4$  for 32 minutes. 16 min after the injection lemon juice (2 ml) was given orally. Time activity curves were generated to evaluate the uptake and secretion pattern.

All patients reported a definite improvement in joint pain and dryness of the mouth and eyes. ESR and CRP decreased significantly during the treatment period. Saliva formation and secretion, as detected by salivary glands scintigraphy improved (Fig. 1). Given the low number of patients, statistical analysis was not performed. Infliximab was well tolerated and side effects were not observed. No patients had to interrupt the therapy, no opportunistic infections were observed, and no patient became anti-dsDNA antibody positive during treatment. In conclusion our study on a small group of patients indicates that the use of infliximab, in combination with methotrexate or cyclosporin A is safe and effective in improving symptoms and salivary gland function. Salivary gland scintigraphy can monitor the efficacy of immune treatment on residual salivary function. Moreover, by repeating the scintigraphy at different time points, we may be able to identify the optimal duration and dosage of therapy for cost-effective treatment. These results suggest that infliximab could have a role in the treatment of patients with Sjögren's syndrome and studies in a larger series of patients are needed.

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### References

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### Bleeding tendency and relapsing small vessel thromboses in a patient with secondary antiphospholipid syndrome

Sirs,

We would like to present the complex clinical case of a female patient who originally suffered from both haemorrhagic diathesis due to multiple coagulation defects and primary antiphospholipid syndrome (PAPS), was later diagnosed with systemic lupus erythematosus (SLE), and finally succumb-