Sialorrhoea as early oral clinical manifestation of primary Sjögren's syndrome?

Sirs, Sjögren's syndrome (SS) is a systemic autoimmune exocrinopathy that affects the salivary and lacrimal glands, typically presenting as the 'sicca complex' of dry eyes (xerophthalmia) and dry mouth (xerostomia). It is generally accepted that SS diagnosis should be based on several clinical and laboratory findings. At present, even though the high validity and reliability of the classification criteria proposed and recently revised by the European Community Study Group has been reported, there is still a lack of international consensus. This situation, in addition to the observation that the initial clinical manifestation of SS is often non-specific and vague, frequently leads to a delay in diagnosis that, in some cases, can be as long as 11 years, with serious consequences in proper management of the diseases and prevention of potential complications. We observed four patients whose histological features and laboratory data suggested that they were suffering from SS, but with initial clinical findings that did not fulfil European diagnostic criteria and did not allow us to make a prompt and early diagnosis. In fact, in each patient we observed the presence of a symptom that is very infrequent in the general population and has never been described in SS but, on the contrary, seems to strongly contrast with traditional clinical features of SS: the occurrence of sialorrhoea.

All patients (Table 1) presented to our Department of Oral Medicine with a history of increased, excessive salivary flow, in the absence of any other local or systemic symptoms. They reported a long-term overproduction of saliva causing a nightly soiling of clothes and bed linens and daily embarrassing dysfunction and distortions in speech and swallowing. Clinical examination revealed an excessive saliva production in the absence of any other pathological signs. We did not perform sialometry because saliva collection is a well-recognized diagnostic tool in patients affected with xerostomia; however, no scientifically accepted diagnostic test is available in patients with hypersalivation.
excluding all the recognized causes of sialorrhoea, such as local irritations, heavy metal poisoning, drugs, mental retardation or other neurologic disorders [4], we performed routine laboratory investigations. Furthermore, since salivary gland functionality can be involved in several infectious and autoimmune diseases, we included in the workup hepatitis C virus, HIV, cytomegalovirus, Epstein–Barr virus antibodies and antinuclear serum antibodies (ANA). Surprisingly the results showed, in all patients, the presence of ANA, Ro(SS-A) and La (SS-B) antibodies. Since antibodies to the ribonuclease protein antigens Ro(SS-A) and La(SS-B) are a well-recognized feature of SS, we subsequently performed lower lip biopsy which revealed focal sialoadenitis of minor salivary glands (focus score \( \geq 1 \)) [5]. According to European criteria, these patients could not be diagnosed as having SS. After a mean time of 8 months, all patients gradually developed the traditional symptoms of dry mouth and dry eyes, and in two cases enlargement of the parotid glands occurred, allowing us to make a definitive, if delayed, diagnosis of SS.

Further studies are required; it is our opinion that sialorrhoea might represent, in certain cases, an early clinical feature of SS. We hypothesize that the lymphocytic infiltration, in its early phases, might cause, via cytokine secretion, an alteration of the salivary gland function that might be expressed clinically as an increased salivary flow. The destruction of the glandular acinar units might occur subsequently, leading to the traditional clinical feature of xerostomia with a reduction of salivary secretion. In fact, several studies have analysed the efficacy of certain cytokines, mainly human interferon (IFN-)\(x\) and recombinant IFN-\(\alpha\)-2 [5], to improve salivary function in patients with SS, and Smith et al. [6] have demonstrated that IFN-\(x\) regulates the gene expression of the water channel aquaporin-5 in human parotid glands. With regard to this, it is possible that the exposure to lymphocyte-derived IFN-\(x\) could increase salivary flow rate in SS early phases. On the other hand, several other cytokines, mainly interleukin (IL)-2, IL-6, interferon-\(\gamma\) (IFN-\(\gamma\)) and tumor necrosis factor (TNF)-\(\alpha\), have been associated with increased DNA degradation of human salivary gland cell line, cell death and subsequent inflammatory destruction of salivary glandular tissue with a decrease in saliva production [7, 8]. Thus, it is possible that destruction of the glandular acinar units might occur subsequently as a consequence of the exposure to different cytokines. Furthermore, it is important to note that other authors have also underlined that the natural history of SS could be characterized, in its early stage, by salivary glands dysfunctions occurring long before xerostomia/hyposalivation: changes in sialochemistry, leading in some cases to early dental loss, and recurrent parotid swelling preceding dry mouth by several years have been previously reported in the American, European and Chinese literature [9]. In conclusion, we suggest that sialorrhoea might be an early symptom of SS, and that SS should be taken into account in differential diagnosis of patients complaining of sialorrhoea. The present case report has been presented as a poster at the First International Congress on Sialivary Gland Diseases, 27–30 January 2002, Geneva, Switzerland. The abstract has not been published.

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Table 1. Patients’ personal and clinical data

<table>
<thead>
<tr>
<th>Patients</th>
<th>Age</th>
<th>Sex</th>
<th>Onset of sialorrhoea (months before patient’s examination)</th>
<th>Development of xerostomia (months after laboratory/histological investigations)</th>
<th>Diagnostic delay (months)</th>
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