

Forget the mouth what about the rest of me?

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Introduction

Approximately 70% of patients with Sjögren's Syndrome will have extra-glandular symptoms in addition to the mouth and eye dryness at some point in the course of their condition.

Fatigue

Physical and mental fatigue is common in patients with Sjögren's. Studies confirm significantly higher levels of fatigue than healthy controls with similar levels of mental and physical fatigue to those affecting patients with other connective tissue diseases such as Systemic Lupus Erythematosus (Bowman et al Rheumatology 2004)

Lung disease

Many patients complain of a chronic cough, which is almost certainly related to drying of the mucous membranes. Sometimes pilocarpine treatment helps relieve this. More serious lung disease is unusual. Occasional patients have been described with interstitial fibrosis (a chronic low grade inflammation of the lungs) or lymphocytic interstitial pneumonitis (LIP) which causes acute inflammation in the lungs and X-Ray changes. One study looked at a series of 50 patients with Sjögren's Syndrome and found X-Ray abnormalities in 14% and abnormalities on scanning on 34% but only 26% had symptoms and the majority of these were mild (Franquet et al, AJR 1997).

Thyroid disease

Thyroid Disease is common in the normal population affecting up to 11% of females over the age of 60 years. Thyroid disease, most commonly hypothyroidism (underactive thyroid), accompanies Sjögren's Syndrome in about 20% of cases. Thyroid autoantibodies (protein markers of disease) are present in 20-30% of patients with Sjögren's and may be slightly more common in the Ro/La negative group (Davidson et al Rheumatology 1998). Another interesting observation is that 37% of patients with autoimmune thyroid disease have an objective dry mouth and 23% have objective dry eyes (Coll et al J Rheumatol. 1997 Sep;24(9):1719-24)

Urinary tract symptoms and urinary tract infection (UTI)

Symptoms of urinary dysfunction such as urinary frequency and discomfort are fairly common in normal women. They are however increased in patients with Sjögren's Syndrome. A study by Haarala and colleagues (2000) found mild urinary symptoms in 61% of patients with Sjögren's compared with 27% of women without. Severe symptoms were seen in 14% and 7% respectively. Overall 27% of Sjögren's patients report urinary frequency and 36% complain of suprapubic pain. Infection should be excluded in the first instance, and if present treated appropriately with an appropriate antibiotic. A few patients with recurrent urinary tract infection benefit from taking regular, low dose antibiotic therapy.



In general good hydration levels should be maintained and some patients report benefit from drinking cranberry juice, which has the effect of alkalising the urine. A similar effect can be achieved using potassium citrate mixture – available via pharmacies in various commercial preparations e.g. cymalon, cystopurin.

The frequency of urinary tract infection (UTI) in patients with Sjögren's Syndrome is not accurately known but in general is probably higher than expected within the normal population. Certainly in patients with Rheumatoid Arthritis the frequency of recurrent UTI is increased if the patient also has Sjögren's from 6% in those with Rheumatoid alone to 30% in those with co-existent Sjögren's (Tischler et al 1992).

Vaginal dryness and dyspareunia

Vaginal dryness affects 76% of women with Sjögren's compared to 5% of those without (Lehrer et al 1994) and dyspareunia (pain on intercourse) is a problem in 40%. Microscopic examination of the vaginal lining tissue shows evidence of inflammation (Skopouli et al 1994). Treatment of vaginal dryness includes the use of lubricating gels to aid intercourse (e.g. KY jelly) and longer acting vaginal moisturisers to improve moisture levels within the vagina (e.g. Replens or Sylk, both available over the counter from pharmacies). Recurrent Candida infection (thrush) is common and can affect the mouth or vagina. Anything that improves moisture levels will help. Interestingly rates of oral

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candida infection fall in patients who start pilocarpine (Rhodus et al) and as some patients on pilocarpine report improved vaginal moisture levels it is possible it has a beneficial effect on vaginal candida too.

Vaginal candidiasis (Thrush)

Vaginal Candidiasis (Thrush) is caused by overgrowth of the fungus candida albicans. This fungus is found in small amounts on the mucous membranes of the mouth and genital area of normal people but in the right conditions can multiply and cause problems. This is frequently seen in the dry conditions found in Sjögren's patients and can prove resistant to treatment. One study found evidence of candida in 80% of patients with Sjögren's (Rhodus et al). Simple creams and pessaries may be beneficial in some e.g. Clotrimazole (available over the counter or on prescription), although oral fluconazole may be needed in more resistant cases. It is important to maintain moisture levels and treat partners too if you are sexually active.

Interstitial cystitis

Interstitial cystitis is a chronic inflammatory bladder disease of uncertain cause. 90% of sufferers are female. It causes chronic inflammation of the bladder wall but in the absence of proven infection. No single treatment is universally effective and management includes good hydration and the use of anti-histamines. Some women find cimetidine helpful and both steroids and cyclosporine have been used. Some urologists treat it with bladder instillations. Two are available – Dimethyl sulphoxide (Rimson-50) and Sodium hyaluronate, but both require expert supervision. There is no good data on the prevalence of interstitial cystitis in Sjögren's Syndrome although anecdotal reports suggest it is common. In one small study of 10 patients with interstitial cystitis 2 were found to have Sjögren's and 6 of the others had sicca symptoms (Van der Merwe et al). In a more recent follow-up study the same authors suggest that Sjögren's is present in 23% of all patients with interstitial cystitis.

Renal involvement

Renal disease impacting on the quality of the life or kidney function is rare but mild abnormalities of kidney function can be detected in about 50% of patients with Sjögren's Syndrome.

A study of patients with Sjögren's Syndrome in Finland revealed that mild proteinuria (the presence of more than 1.5 g of protein in the urine over a 24 hour period) was common (44%) but almost always asymptomatic. In the same study Renal Tubular acidosis was found in 33%. This is a condition where the tubules of the kidney are affected in such a way that they are unable to maintain the normal acid:alkali balance of their urine. In the majority of people it is asymptomatic but it can predispose towards kidney stones. Treatment when required is with bicarbonate to restore the urine pH. There is also a trend for those with renal involvement to have higher Blood pressure than those without (Pertovaara et al 1999).

Dysphagia and oral candida

There are many potential causes of swallowing difficulties (dysphagia) in Sjögren's Syndrome. The oral dryness can make chewing and swallowing difficult and these problems are exacerbated if dental disease has led to loss of some or all of the natural teeth. The saliva not only reduces in volume but changes in quality and many patients need to drink water to help swallowing. Several studies have shown changes in the muscular contractions within the oesophagus (food gullet) which may hamper swallowing and one study found evidence of an oesophageal web in 10% of patients with Sjögren's. These webs consist of an elastic membrane of oesophageal mucosa – the tissue normally lining the gullet. Oral candida (thrush) is a common problem and may affect up to 75% of patients

with Sjögren's at some point in their illness and can contribute to oral symptoms. The management of candida has been comprehensively discussed in a previous newsletter article (John Hamburger and Stephen Porter, Summer 2006, Vol 20, issue 2).

Irritable bowel syndrome

Irritable bowel syndrome is a poorly understood condition characterised by the presence of bloating, intermittent diarrhoea and abdominal colic, which may be relieved by a bowel action. It is thought to affect up to 20% of the general population at some time and is slightly commoner in women. There is no diagnostic test – the diagnosis is often made on the presence of classical symptoms and absence of other causes. In many patients the symptoms are chronic. There are no studies looking at the prevalence of irritable bowel syndrome in patients with Sjögren's Syndrome but anecdotal reports suggest it is common. Dietary change including increasing the fibre content of the diet may help.

Gastritis

Dyspepsia (heartburn and indigestion) is a common symptom in the normal population. There is a known association in the general population between the presence of infection with bacteria known as helicobacter pylori and the presence of indigestion and ulcers. Helicobacter pylori infection rates are similar in patients with Sjögren's Syndrome and the normal population (57% v 62%) but whereas eradication of the bacterial infection cured the symptoms in the normal patients it did not have a similar effect in the Sjögren's patients (Sorrentino et al).

Coeliac disease

Coeliac disease is an intolerance to gluten (a wheat protein) and leads to malabsorption. Common symptoms include weight loss and anaemia and simple screening blood tests are usually helpful in confirming a diagnosis. Evidence of coeliac disease was found in 4.5% of patients with Sjögren's Syndrome in one Hungarian study (Szodary et al, 2004). This compares with a prevalence of 4.5 – 5.5 per 1000 in the normal European population. In another study antibodies to tissue transglutaminase (TTG), an antibody strongly associated with coeliac disease, were present in 12% of patients with Sjögren's Syndrome compared to 4% of normal controls. On further investigation over 70% of the anti-TTG positive patients were found to have biopsy evidence of coeliac disease (Luft et al 2003). Overall therefore coeliac disease is ten times commoner in patients with Sjögren's Syndrome than in the normal population. Treatment is with a gluten free diet.

Liver

Mild elevation of liver enzymes are seen in up to a quarter of patients with Sjögren's Syndrome but most of these patients are asymptomatic and more serious disease is rare. In one large study of 300 patients with primary Sjögren's Syndrome some signs of liver involvement were found in 7% of patients but the majority of these were asymptomatic (Skopouli et al, 1994). The commonest associated liver condition is primary biliary cirrhosis (see below). Some patients have mild liver inflammation visible on biopsy which is felt to be a manifestation of the Sjögren's itself but other forms of liver disease are rare and probably associated by chance alone

Primary biliary cirrhosis

Primary Biliary cirrhosis (PBC) is a slowly progressive, inflammatory condition of the liver. There are many similarities between Sjögren's and Primary biliary cirrhosis - both affect primarily women and are thought to be autoimmune. They both cause a similar pattern of inflammation on biopsy. In studies Sjögren's Syndrome is found in about 17% of patients with PBC (Parikh et al, 2001) and conversely PBC has been found in about 6% of patients with Sjögren's. It is probable that there is a true 'overlap' syndrome where patients develop both conditions

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alongside each other. Treatment is usually with ursodeoxycholic acid (UDCA) which can slow the progress of the liver condition and improve the long-term outlook.

Autonomic nervous system dysfunction

The autonomic nervous system controls bodily functions not under conscious control e.g. heart rate, gastric emptying etc. Autonomic nervous system dysfunction is seen in a proportion of patients with Sjögren's Syndrome and can be a factor in bowel disease e.g. gastric emptying is slowed in approximately 70% of symptomatic patients with Sjögren's Syndrome (Kovacs et al, 2003).

Skin

Dry skin affects at least 50% of patients and can cause pruritis (itching). Treatment is with simple moisturisers and avoidance of perfumed products. Two specific types of rashes are seen in patients with Sjögren's Syndrome – Hypergammaglobulinaemic purpura (HGP) and Sub acute cutaneous Lupus (SCLE) – both are commoner in Ro/La + patients. HGP causes a blotchy, reddish, flat rash usually on the lower legs. It is associated with high protein levels in the blood and often responds to treatment with hydroxychloroquine. SCLE is a photosensitive, non-scarring rash, usually on the arms and front of the chest. Treatment includes sun avoidance, the use of a high factor sunscreen and hydroxychloroquine. In a few patients further immunosuppressive drugs are required e.g. azathioprine.

Raynauds

Raynauds – where the blood vessels to the fingers and toes go into spasm - is common in Sjögren's and can be precipitated by exposure to cold and/or vibration. It is critical that sufferers do not smoke as this worsens the condition. Certain drugs e.g. betablockers can also worsen Raynauds and should be avoided if possible. Treatments involve keeping warm, gink biloba and fish oils. In some cases drugs e.g. nifedipine, amlodipine are helpful although side effects may limit their use.

Mental health issues

A recent study has looked at mental health issues in patients with Sjögren's and found high levels of psychological distress compared to healthy controls. Certain personality features (negativity, preoccupation with detail, perfectionism and anxiety) were found more often in patients with Sjögren's than those without (Kariskos et al Rheumatology, 2010).

Summary

Symptoms outside of the eyes and mouth are common in patients with Sjögren's Syndrome.