

Case reports

Auricular chondritis and diffuse proliferative glomerulonephritis in primary Sjögren's syndrome

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SUMMARY Bilateral auricular inflammation with histological changes of relapsing polychondritis was observed in a female patient with primary Sjögren's syndrome. This was accompanied by rapidly progressive renal insufficiency due to diffuse proliferative glomerulonephritis. To our knowledge this is the first well documented case of primary Sjögren's syndrome associated with chondritis and glomerulonephritis, further emphasising the wide spectrum of extraglandular manifestations in this autoimmune disorder.

Primary Sjögren's syndrome is an autoimmune disorder characterised by chronic inflammation of exocrine glands. Recent publications have shown an array of potential extraglandular manifestations, ranging from cutaneous vasculitis to severe central nervous system disease.^{1,2} We report an unusual association of auricular chondritis and diffuse proliferative glomerulonephritis in a patient with primary Sjögren's syndrome.

Case report

A 48 year old housewife first noticed recurrent parotid gland enlargement, malaise, fever, and occasional joint symptoms in 1967. Since 1976 she had had permanent parotid gland enlargement and recurrent crises of facial angio-oedema and urticaria. In 1982 marked xerostomia and lack of saliva discharge after massage of parotid and submaxillary glands were noted. In 1983 she underwent surgery to remove a ductal breast adenocarcinoma followed by treatment with chlorambucil 4 mg and prednisone 20 mg daily. In November 1985 she developed acute

pulmonary oedema secondary to renal failure and was treated with peritoneal dialysis. At this time microhaematuria and proteinuria (>3 g daily) were observed, and a renal biopsy was performed. Light microscopy showed diffuse involvement of glomeruli with enlargement of glomerular tufts, increase of the mesangial matrix, and diffuse mesangioendothelial proliferation with severe narrowing of the intracapillary lumen, hyaline thrombi, and neutrophil infiltrate. The glomerular basement membranes were thickened and showed subendothelial deposits. These deposits were also present in the mesangium. A moderate neutrophil infiltrate and diffuse oedema were observed in the interstitium. No evidence of extracapillary proliferation was observed. Immunofluorescence showed granular mesangial and subendothelial deposits of IgG, IgM, IgA, C1q, and C3.

A diagnosis of diffuse proliferative glomerulonephritis was made and treatment with prednisone 60 mg daily was started and tapered to 5 mg after creatinine concentrations and urine sediment returned to normal. In February 1986 the patient experienced sudden pain, swelling, and reddening of both ears. She was afebrile, with red eyes, dry mouth, and intense erythema and oedema of both

Accepted for publication 19 October 1988.
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Table 1 *In vitro* immunoglobulins and rheumatoid factor production by peripheral blood lymphocytes. Values are mean (SE)

	Unstimulated			Pokeweed mitogen stimulated		
	IgG ($\mu\text{g/l}$)	IgM ($\mu\text{g/l}$)	IgM RF [†] ($\mu\text{g/l}$)	IgG ($\mu\text{g/l}$)	IgM ($\mu\text{g/l}$)	IgM RF ($\mu\text{g/l}$)
Case report	776 (153)*	78 (2)	3.2 (0.1)	337 (83)*	56 (2)*	1.6 (0.1)
Patients with primary SS [†] (n=15)	1376 (432)	268 (83)	18 (7)	1370 (508)	591 (177)	16 (10)
Normal controls (n=15)	247 (32)	40 (15)	2.7 (0.7)	2657 (679)	861 (162)	1 (0.4)

B cells (0.5×10^5) were cultured in triplicate in complete medium containing RPMI 1640, fetal calf serum 10%, L-glutamine and antibiotics and tested for spontaneous immunoglobulin and rheumatoid factor production after seven days. When cultures were stimulated with pokeweed mitogen (diluted 1/200) T cells (0.5×10^5) were also added. Concentrations of immunoglobulin and rheumatoid factor were determined by enzyme linked immunosorbent assay (ELISA).

* $p < 0.01$ as compared with normal controls (paired Student's *t* test).

[†]RF=rheumatoid factor; SS=Sjögren's syndrome.

external ears with typical 'beefy' appearance. There was no evidence of nasal or laryngeal involvement. An ear lobe biopsy specimen showed loss of cartilage basophilic staining, intense lymphocytic infiltration, and areas replaced by fibrous tissue compatible with relapsing polychondritis.³ A heavy mononuclear cell infiltrate with minor salivary gland tissue gave a focus score of 12 according to criteria of Greenspan *et al.*⁴ Schirmer's test and rose bengal stain were both positive. Signs of ear inflammation abated after increasing prednisone to 30 mg daily but recurred one month later when an attempt was made to decrease the dose. Laboratory tests showed haemoglobin 118 g/l, packed cell volume 0.38, Westergren erythrocyte sedimentation rate 40 mm/h. The rheumatoid arthritis test (latex test, dilution 1/640), cryoglobulins, antinuclear antibodies (indirect immunofluorescence on fibroblasts), and anti-SSA antibodies (double immunodiffusion) were positive. Anti-Sm, anti-RNP, and complement levels (CH₅₀, C3, and C4) were negative or normal. Anti-DNA antibodies were persistently negative when tested by the *Crithidia luciliae* and Farr assays. The lymphocyte phenotypic profile was determined by indirect immunofluorescence with specific monoclonal antibodies as described previously.⁵ Peripheral blood mononuclear cells contained CD3 (+) 48% (control 55 (SEM 2)%, n=14); CD4 (+) 29% (control 43 (3)%); CD8 (+) 31% (control 21 (3)%), Mo1 (+) 43% (control 21 (3)%), CD4/CD8 ratio 0.93 (control 2.19 (0.3)). We examined immunoglobulin production *in vitro* by methods previously described in detail⁵ (Table 1). Spontaneous IgG synthesis was significantly increased compared with controls. IgG and IgM syntheses stimulated by pokeweed mitogen were lower than those of controls. Levels of IgM RF in unstimulated and stimulated cultures were similar to those of controls

and lower than those of the other patients with primary Sjögren's syndrome.

One year after the initial episode the patient was asymptomatic with normal creatinine clearance but again showing urine sediment abnormalities—namely, microhaematuria and proteinuria 900 mg/24 h. There was no evidence of recurrent ear inflammation or deformity. Other laboratory measurements remained unchanged except for disappearance of cryoglobulins. The patient remains well taking prednisone 2.5 mg daily.

Discussion

Our patient meets diagnostic criteria for primary Sjögren's syndrome⁶ as shown by her typical history of recurrent parotitis, xerophthalmia, xerostomia, and an intense chronic mononuclear cell infiltrate in salivary glands. Additionally, she had immunological variables suggesting an autoimmune process—namely, antinuclear antibodies, rheumatoid factor, cryoglobulins, and anti-SSA antibodies. The emergence of ductal breast adenocarcinoma may reflect the predisposition to malignancy in patients with Sjögren's syndrome.¹ The phenotypic lymphocyte profile showing decrease of the helper/inducer (CD4+) and relative increase of the cytotoxic/suppressor (CD8+) T cell subpopulation in peripheral blood is consistent with our previous report.⁵ This pattern suggests redistribution of T helper cells to affected organs as observed in immunohistological studies.¹ Also, a higher spontaneous IgG production by peripheral blood mononuclear cell cultures indicates hyperactive B cell responses, as shown previously in a larger group of patients.⁵ This may be relevant to the associated chondritic process, where IgG anticollagen antibodies and immune

complexes deposited in cartilage have been described.⁷ The patient showed a diminished pokeweed mitogen induced immunoglobulin synthesis, as we have observed in primary Sjögren's syndrome⁵ and rheumatoid arthritis (unpublished data). It is possible that in the presence of B cell hyperactivation pokeweed mitogen may have an inhibitory effect, as previously reported in patients with systemic lupus erythematosus.^{8,9}

Our patient does not meet criteria for systemic lupus erythematosus¹⁰ or any other connective tissue disease, and the anti-Sm and anti-DNA antibodies were persistently negative. The histological findings in ear cartilage are highly suggestive of relapsing polychondritis.³ At present this diagnosis cannot be sustained, however, as only a single episode has occurred and no signs of extended cartilage inflammation have been seen.³ Rapidly progressive glomerulonephritis has been described in patients with relapsing polychondritis,¹¹⁻¹³ with a predominant pattern of severe extracapillary proliferation and crescent formation. Our patient showed a typical pattern of proliferative diffuse glomerulonephritis, and the severity of the lesion is emphasised by the presence of hyaline thrombi. This finding may explain the sudden development of transitory renal insufficiency.¹⁴ Moutsopoulos *et al* reported three cases with immune complex mediated glomerulonephritis in patients with longstanding sicca syndrome, and, as in our case, two of them showed cryoglobulins.¹⁵ Thus it is possible that the renal lesion in our patient may be related to cryoglobulinaemia.

In summary, we report an unusual association of ear chondritis and diffuse proliferative glomerulonephritis in a patient with primary Sjögren's syndrome, illustrating the potential risk of severe renal compromise in these patients. Further, cartilage inflammation must now be added to the growing list of extraglandular manifestations in primary Sjögren's syndrome.

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