Systemic sclerosis associated with primary biliary cirrhosis (Reynolds' syndrome) in a pair of siblings

Sirs,

Reynolds' syndrome is characterized by the presence of primary biliary cirrhosis (PBC) associated to systemic sclerosis or its variants. Since its original description (1), few series have been reported (2-6), with more than 95% of all cases being females. Although the family susceptibility to autoimmunity in patients with PBC is well known, there are not any descriptions in the English literature of systemic sclerosis associated with PBC in siblings. Herein, we describe two siblings, brother and sister, who suffered this dual autoimmunity.

Case 1. A 58-year-old nun who, upon entering our institute in 1986, described a 17-year history of Raynaud's phenomenon. Fifteen years later, she noticed telangiectasia in the face and hands as well as progressive functional limitation in hands, and ulcers in both elbows. She also referred a seven-month epigastric pain with intermittent nausea, vomiting and diarrhea, and generalized pruritus. No previous treatment was prescribed. Physical examination showed scleral icterus, disseminated telengiectasia, acrosclerosis and calcinosis plaques with ulceration in both elbows. Laboratory analyses are shown in Table I. A hepatic biopsy showed portal triads infiltrated with lymphocyte as well as destruction of bile ducts. Radiographic studies documented pulmonary fibrosis. Limited scleroderma and PBC (Reynolds' syndrome) was diagnosed and treatment with colchicine and nifedipine was started. During the next three years, the patient developed severe pulmonary hypertension and died in 1989.

Case 2. The second case is that of her 55-year-old brother, a catholic priest who noted, since 1994, Raynaud's phenomenon as a sole manifestation. Four years later, he developed telangiectasia in the face, upper part of the chest and hands, and he further noticed a slow and progressive swelling of his fingers. The following year he showed lower dysphagia to solids. Physical examination showed acrosclerosis in the hands with giant loops and avascular areas detected through capilaroscopy. Laboratory analyses are shown in Table I. A hepatic biopsy showed fibrosis in septa link adjacent portal triads and some regenerative nodules. The radiographic study showed calcifications in the second and third right fingertips. The patient was treated with colchicine and losartan and remained stable for the following five years, after which he showed upper digestive tract hemorrhage secondary to rupture of esophagi varicose veins. He developed hepatic encephalopathy and died in 2004.

Table I. Laboratory values.

	Case 1	Case 2
Bilirubin (mg/dL)		
Total	2.9	1.2
Conjugated	1.7	0.1
Alkaline phosphatase (U/L)	712	582
Aspartate aminotransferase (U/L)	101	70
Alanine aminotransferase (U/L)	55	71
Albumin (g/dL)	3.3	3.9
Rheumatoid factor (latex)	1:10240	ND
Anti-smooth-muscle antibodies	Positive 1:160	ND
Antimitochondrial antibodies	Positive, 1:160	Positive, 1:160
Anti-centromere antibodies	Positive 1:160	Positive 1:160

The presence of antimitochondrial antibodies in more than 90% of cases, a familial clustering and the presence of immunological abnormalities in family members suggests that PBC has an autoimmune aetiology. Selmi *et al*. (6) described PBC in five of eight sets of monozygotic twins. This pairwise concordance rate (0.63) is the highest reported among autoimmune diseases. However, based on the discordant pairs, its clear that either epigenetic and/or environment play a critical role. On the other hand, familial scleroderma has been reported in five families with two affected members; however, a common HLA haplotype was not found (7). The greater family propensity to autoimmunity in these patients could be interpreted as a reflection of sharing susceptibility genes or, quite the opposite, that several members of a family could have shared exposure to the same infectious or environmental agent. The association of PBC and scleroderma has been reported in between 3% and 50% of all PBC cases. In the largest series reported to this day, Rigamonti *et al*. (8) identified 43 cases of PBC with scleroderma in their database of 580 PBC patients (7.4%). Ninety-three percent were women and likewise 93% had limited scleroderma. Hepatic damage in these cases progressed more slowly when compared with controls. However, they did not describe a family association.

The cases reported herein are interesting because they are the first pair of siblings with Reynolds' syndrome described in the English literature.

J. JAKEZ-OCAMPO, *MD*
Y. ATISHA-FREGOSO, *MD*
L. LLORENTE, *MD*

Department of Immunology and Rheumatology, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán.

Address correspondence to: Dr. Luis Llorente, Department of Immunology and Rheumatology, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán
Vasco de Quiroga 15, Tlalpan, 14000 México, D.F., México.
E-mail: lllyrp@quetzal.innsz.mx

Competing interests: none declared.

References

1. REYNOLDS TB, DENISON EK, FRANKL HD, LIEBERMAN FL, PETERS RL: Primary biliary cirrhosis with scleroderma, Raynaud's phenomenom and telangiectasia. *Am J Med* 1971; 50: 302-12.
2. O'BRIAN ST, EDDY WM, KRAWITT EL: Primary biliary cirrhosis associated with scleroderma. *Gastroenterology* 1972; 62: 118-21.
3. POWELL FC, SCHROETER AL, DICKSON ER: Primary biliary cirrhosis and the CREST syndrome: a report of 22 cases. *Q J Med* 1987; 62: 75-82.
4. MARASINI B, GAGETTA M, ROSSI V, FERRARI P: Rheumatic disorders and primary biliary cirrhosis: an appraisal of 170 Italian patients. *Ann Rheum Dis* 2001; 60: 1046-9.
5. WATT FE, JAMES OFW, JONES DEJ: Patterns of autoimmunity in primary biliary cirrhosis patients and their families: a population-based cohort study. *Q J Med* 2004; 97: 397-406.
6. SELMI C, MAYO MJ, BACH N *et al*.: Primary biliary cirrhosis in monozygotic and dizygotic twins: genetics, epigenetics and environment. *Gastroenterology* 2004; 127: 485-92.
7. MANOLIOS N, DUNCKLEY H, CHIVERS T, BROOKS P, ENGLERT H: Immunogenetic analysis of 5 families with multicase occurrence of scleroderma and/or related variants. *J Rheumatol* 1995; 22: 85-92.
8. RIGAMONTI C, SHAND LM, FEUDJO M *et al*.: Clinical features and prognosis of primary biliary cirrhosis asociated with systemic sclerosis. *Gut* 2006; 55: 388-94.