Development of fulminant hepatitis B (precore variant mutant type) after the discontinuation of low-dose methotrexate therapy in a rheumatoid arthritis patient. *Arthritis Rheum* 2001; 44: 339-42.
8. CARMAN WF, JACYNAMR, HADZIYANNIS S *et al*.: Mutation preventing formation of hepatitis B e antigen in patients with chronic hepatitis B infection. *Lancet* 1989; 2: 588-91.
9. BUCKWOLD VE, XU Z, CHEN M, YEN TSB, OU J: Effects of a naturally occurring mutation in the hepatitis B virus basal core promoter on precore gene expression and viral replication. *J Virol* 1996; 70: 5845-51.
10. SATO S, SUZUKI K, AKAHANE Y *et al*.: Hepatitis B virus strains with mutations in the core promoter in patients with fulminant hepatitis. *Ann Intern Med* 1995; 122: 241-8.

## Silicone gel filled breast implants and dermatomyositis

Sirs,

Several studies have investigated the possible relationship between silicone gel-filled breast implants and autoimmune or connective tissue diseases (1-4). From a public health perspective, there appears to be no significant evidence that such a relation exists (5). Nevertheless, the coexistence of breast implants and connective tissue disease in a number of individuals points to a causal relationship; silicone bleeding from silicone-gel filled breast implants could act as a precipitating factor for the development of these diseases (6). We report herein two women with common HLA alleles, who presented with dermatomyositis and anti-synthetase antibodies after the implantation of silicone-gel-filled breast prostheses. This association has rarely been reported previously (7, 8).

*Case 1*. A 40-year-old white woman presented with symmetrical proximal muscle weakness of the limb girdles and neck in September 1997. Six months earlier the patient had undergone surgical breast augmentation for cosmetic reasons, with the implantation of bilateral silicone gel-filled breast prostheses. A left deltoid muscle biopsy showed perifascicular atrophy, necrosis and inflammatory infiltrate. Anti-synthetase (anti-Jo-1) antibodies were found by ELISAand confirmed by immunoprecipitation of RNAs from $^{32}$P-labeled HeLa extracts. The patient was treated with prednisone (1mg/kg/day) with mild improvement, but elevated creatine phosphokinase persisted over the next 8 months; azathioprine (1.5 mg/kg/d) initially and later cyclosporine (5 mg/kg/d) had to be added to the patient's treatment. Despite this drug therapy, mild weakness and high creatine phosphokinase level persisted, so the prostheses were explanted on July 1999. The patient is now being treated with cyclosporine (3 mg/kg/d) and prednisone 5 mg/d and is asymptomatic. High-resolution computerized tomography (HRCT) has detected no lung involvement and pulmonary function tests are normal. The patient's HLA was HLA-A [1, 23]; HLA-B [8(Bw6), 44(Bw4)]; HLA-Cw [07, 04]; HLA-DRB1* [0301(HLA-DRB3* 0101), 07(HLA-DRB4*)]; HLA-DQB1* [0201, 0202].

*Case 2*. A 51-year-old woman was admitted for evaluation of arthralgia and erratic arthritis of the metacarpophalangeal joints, asthenia and myalgia. Eight years before she had undergone breast augmentation with silicone-gel filled implants for cosmetic reasons. Gottron papules were observed on the skin of the hands and elbows and a periorbitary edema with heliotrope rash of the eyelids was also noted. Skin retraction and local changes at the implantation site with contracture around the implant were observed on physical examination of the breast region. Muscle biopsy showed characteristic findings of dermatomyositis. Anti-synthetase (anti-Jo-1) antibodies were positive. The patient's HLA was HLA-A [1, 24]; HLA-B [8(Bw6), 39(Bw6)]; HLA-Cw [07, 12]; HLA-DRB1* [0301 (HLA-DRB3* 0101), 16 (HLA-DRB5*)]; HLA-DQB1* [0201, 0502]. Corticosteroid treatment (1 mg/kg/d) was initiated, but azathioprine at a dose of 1.5 mg/kg/d had to be added to improve clinical status. She was counseled to undergo explantation of the breast prostheses, but she repeatedly refused. Aggressive treatment with prednisone boluses (1 g/day, for 3 days) and the first of a series of 6 monthly cyclophosphamide boluses (750 mg) was initiated with apparent good response. At this time HRCT showed calcification and retraction of the prosthesis and mild lung fibrosis. Respiratory function tests disclosed a moderate restrictive pattern.

Silicone gel breast prostheses are extensively utilized for breast augmentation or reconstruction. We have had the opportunity to diagnose and attend two patients with silicone-gel filled breast implants who developed full-blown dermatomyositis after breast augmentation. Both tested positive to anti-synthetase antibody, a specific myositis antibody, but only the patient who refused prosthesis explantation developed a full-blown anti-synthetase syndrome with interstitial lung disease.

The HLA status of these patients showed that class II HLA(DR, DQ) was identical in one of two haplotypes. On the basis of the combination of factors found in the study of these two patients, we speculate that the identical class II HLA alleles resulted in a reaction to silicone that triggered a humoral autoimmune response and the development of full-blown dermatomyositis with anti-synthetase antibodies.

A. SELVA-O'CALLAGHAN[1], *MD, PhD*
J.M. TURA[2], *PhD*
J.M. GRAU-JUNYENT[3], *MD, PhD*
M. LABRADOR-HORRILLO[4], *MD, PhD*
R. SOLANS-LAQUE[1], *MD, PhD*
M. VILARDELL-TARRÉS[1], *MD, PhD*

*[1]Internal Medicine Department and [4]Autoimmune Research Unit, Vall d'Hebron General Hospital; [2]Institut de Recerca Cardiovascular de Barcelona-Csic; [3]Grup d'Investigació Muscular, Hospital Clinic Provincial, Institut d'Investigacions Biomédiques August Pi i Sunyer (Idibaps); Barcelona, Spain.*

*Address correspondence to: Dr Albert Selva-O'Callaghan, C/ Siracusa no. 12 Bis "A", Barcelona 08012, Spain.*
*E-mail: aselva@hg.vhebron.es*

### References

1. BRIDGES AJ, CONLEY C, WANG G, BURNS DE, VASEY FB: A clinical and immunologic evaluation of women with silicone breast implants and symptoms of rheumatic disease. *Ann Intern Med* 1993; 118: 929-36.
2. GABRIEL SE, O'FALLON M, KURLAND LT, BEARD CM, WOODS JE, MELTON J: Risk of connective-tissue diseases and other disorders after breast implantation. *N Engl J Med* 1994; 330: 1697-702.
3. SÁNCHEZ-GUERRERO J, COLDITZ GA, KARLSON EW, HUNTER D, SPEIZER FE, LIANGMH: Silicone breast implants and the risk of connective-tissue diseases and symptoms. *N Engl J Med* 1995; 332: 1666-70.
4. NYRÉN O, YIN L, JOSEFSSON S *et al*.: Risk of connective tissue disease and related disorders among women with breast implants: a nation-wide retrospective cohort study in Sweden. *BMJ* 1998; 316: 417-22.
5. JANOWSKY EC, KUPPER LL, HULKA BS: Meta-analysis of the relation between silicone breast implants and the risk of connective tissue diseases. *N Engl J Med* 2000; 342: 781-90.
6. GAUBITZ M, JACKISCH C, DOMSCHKE W, HEINDEL W, PFLEIDERER B: Silicone breast implants: correlation between implant ruptures, magnetic resonance spectroscopically estimated silicone presence in the liver, antibody status and clinical symptoms. *Rheumatology* 2002; 41: 129-35.
7. HOUPT HR, SONTHEIMER RD: Autoimmune connective tissue disease and connective tissue disease illness after silicone gel augmentation mammoplasty. *J Am Acad Dermatol* 1994; 31: 626-42
8. MEYER DR, BUI HX, CARLSON JA *et al*.: Silicon granulomas and dermatomyositis-like changes associated with chronic eyelid edema after silicone breast implants. *Ophtal Plast Reconstr Surg* 1998; 14: 182-8.