# Letters to the Editor

## Anti-Ro/SSA autoantibodies over time in mothers of children with congenital complete heart block

Sir,

It is commonly assumed that the titer of anti-Ro/SSA antibodies remains stable over the years, but data in the literature are scanty (1-4). Congenital heart block (CHB) is a multidisciplinary field; although anti-Ro/SSA antibodies appear to be pathogenically linked to it (5-7), the cardiological literature often describes CHB mothers presumed to be anti-Ro/SSA negative (8). The aim of this study was to follow the titers of anti-Ro/SSA antibodies in 11 CHB mothers over a long period of time to see whether they remained stable and whether any of the mothers' titers turned negative over time.

CHB was detected *in utero* or at birth. Table I shows the year of each index delivery. Sera were first available in 1989, and from then on sera were tested serially. Antibodies to Ro/SSA were determined by counterimmunoelectrophoresis (CIE) and immunoblotting using a human spleen extract as substrate, as previously described (9). The fine specificity and the titer of the anti-Ro response were also determined by ELISA against 52 and 60 kD recombinant proteins (Eurodiagnostica B.V., Arnhen, The Netherlands).

The results of our study are shown in Table I. Eight out of 11 sera were positive by CIE when first tested. Seven of these 8 remained positive, while only the patient with a very weak 1:2 anti-Ro titer lost the precipitin. Semiquantitative evaluations of anti-Ro titers by CIE showed slight fluctuations in each patient. Serial testing detected variations in the titer not greater than two dilutions. All 8 sera which were positive on IB showed reactivity to the 52 kD protein, 6 being isolated and 2 being associated with anti-60 kD reactivity. All of the sera were initially positive by 52 kD Ro ELISA. Anti-60 kD Ro ELISA was initially positive in 6 mothers, but during the follow-up 4 became negative, although CIE remained positive with stable titers.

As is usual in CHB, the mothers we studied for the most part had only minor symptoms (arthralgias, dry eyes, and photosensitivity) and as a group they remained clinically stable over time. Therefore we could not relate fluctuations in the titers to clinical events. Overall, 10 out of 11 mothers remained positive for anti-Ro/SSA antibodies. However, this was true only when a wide panel of assays was employed. One mother who was positive at a low titer for anti-52 kD eight years after delivery became negative three

**Table I.** Successive anti-Ro/SSA antibody titers in 11 CHB mothers.

| Mother | Index delivery | Serum dates | CIE | Anti-Ro/SSA titer by CIE | IB | ELISA Ro52 kD* | ELISA Ro60 kD° |
|---|---|---|---|---|---|---|---|
| BE | 1969 | 04.17.89 | Ro+La | 1:16 | 52 kD | 74 | 14 |
| | | 11.17.89 | | 1:32 | | 61 | 10 |
| | | 30.09.93 | | 1:16 | | 63 | 15 |
| | | 07.05.94 | | 1:16 | | 44 | 12 |
| | | 06.11.96 | | 1:8 | | 51 | 11 |
| | | 03.09.98 | | 1:16 | | 36 | 8 |
| FR | 1976 | 03.15 89 | Ro | 1:2 | 52 kD | 972 | 33 |
| | | 08.08.91 | Neg | Neg | | 87 | 9 |
| | | 08.25.94 | Neg | Neg | | 68 | 2 |
| | | 04.16.98 | Neg | Neg | | 45 | < 1 |
| Fl | 1976 | 06.12.92 | Ro+La | 1:64 | 52 kD | > 4000 | 25 |
| | | 07.15.94 | Ro | 1:64 | | > 4000 | 22 |
| | | 09.21.95 | | 1:64 | | > 4000 | 19 |
| | | 04.17.98 | | 1:32 | | > 4000 | 12 |
| GC | 1970 | 09.09.91 | Neg | | Neg | 105 | 9 |
| | | 07.05.94 | Neg | | | 71 | 6 |
| | | 06.11.96 | Neg | | | 167 | 5 |
| GE | 1992 | 09.22.92 | Ro+La | 1:16 | 52 kD | 520 | 20 |
| | | 09.30.93 | | 1:16 | | > 4000 | 16 |
| | | 10.06.94 | | 1:16 | | > 4000 | 7 |
| | | 04.24.98 | | 1:16 | | > 4000 | 10 |
| LM | 1992 | 02.22.92 | Ro | 1:128 | 60+52kD | 390 | 12 |
| | | 03.18.93 | | 1:64 | | 527 | 11 |
| | | 09.21.94 | | 1:64 | | 389 | 9 |
| | | 04.20.98 | | 1:64 | | 3520 | 3 |
| MG | 1969 | 07.02.92 | Ro+La | 1:256 | 60+52kD | > 4000 | 177 |
| | | 05.11.93 | Ro+La | 1:128 | | > 4000 | 500 |
| | | 05.30 94 | Ro+La | 1:256 | | > 4000 | 117 |
| | | 01.30.95 | | 1:512 | | > 4000 | 83 |
| | | 10.25.95 | | 1:512 | | > 4000 | 86 |
| | | 06.12.96 | | 1:256 | | > 4000 | 67 |
| | | 04.14.98 | | 1:512 | | > 4000 | 64 |
| MF | 1983 | 02.04.91 | Neg | | Neg | 83 | 13 |
| | | 07.19.94 | Neg | | | 30 | 2 |
| PV | 1960 | 15.04.89 | Neg | | 52 kD | 93 | 12 |
| | | 07.09.91 | Neg | | | 80 | 8 |
| SG | 1972 | 07.05.91 | Ro | 1:4 | | 161 | 21 |
| | | 09.03.93 | Ro | 1:8 | Neg | 238 | 22 |
| | | 07.04.94 | Ro | 1:4 | | 152 | 11 |
| | | 06.11.96 | Ro | 1:8 | | 294 | 16 |
| | | 04.15.98 | Ro | 1:16 | | 218 | 13 |
| TS | 1990 | 04.16.90 | Ro | 1:64 | 52 kD | > 4000 | 53 |
| | | 06.25.91 | Ro | 1:64 | 52 kD | > 4000 | 87 |
| | | 06.02.92 | Ro | 1:32 | | > 4000 | 88 |
| | | 06.29.93 | Ro | 1:128 | | > 4000 | 165 |
| | | 06.14.94 | Ro | 1:128 | | > 4000 | 306 |
| | | 09.11.95 | Ro | 1:128 | | > 4000 | 280 |
| | | 02.13.96 | Ro | 1:256 | | > 4000 | 856 |
| | | 04.16.98 | Ro | 1:128 | | > 4000 | 855 |

* Normal value < 34 AU/ml; °normal value < 16 AU/ml.

years later; this was the only woman who remained asymptomatic throughout the follow-up.

Data in the literature regarding fluctuations in the titer of anti-Ro/SSA antibodies are scanty and conflicting. Some studies have reported a correlation between the changing in anti-Ro titer and disease activity (2-4), but this has not been confirmed by others (1).

Tseng *et al.* (10) studied the immunoblot profile of anti-SSA/Ro and SSB/La antibodies over time in mothers whose children had neonatal lupus, and found that the fine specificity of these antibodies, as assessed by immunoblot, was highly stable for years; no data concerning fluctuations of the antibody titers was given.

Our study therefore represents the first attempt to assess fluctuations in the titer of anti-Ro/SSA antibodies in a group of CHB mothers by ELISA. Our findings hint at some interesting conclusions. First of all, in the majority of this sample of clinically stable anti-Ro/SSA positive mothers, anti-Ro/SSA antibody titers (particularly anti-Ro 52) remained stable over time, and fluctuations were not necessarily related to clinical events. Secondly, the overall positivity for antibodies remained constant over a very long period of time, averaging 19.6 years from the index delivery. Thirdly, and particularly important in the multi-disciplinary field of CHB, anti-Ro/SSA antibodies were persistently positive over the years only when a wide panel of assays was employed, while a more restricted investigation may incorrectly classify the CHB mother as anti-Ro/SSA negative.

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## Bilateral optic neuritis in ankylosing spondylitis

Sir,

Ocular involvement in ankylosing spondylitis is common, particularly in uveitis. It occurs in 25-30% of patients at some point during the course of their disease (1). However, involvement of the retina or optic nerve is very rare. We describe here a patient with ankylosing spondylitis and bilateral optic neuritis.

In April 1992, a 42-year-old woman was seen at the Rheumatology Clinic of Seoul National University Hospital because of low back pain. In 1981, she developed pain in the lower back and buttocks, which improved with the intermittent administration of over-the-counter medications. In early 1992, she visited a hospital due to posterior neck pain which was diagnosed as ankylosing spondylitis.

In April 1992 she was referred to our hospital with pain and stiffness in the neck, middle and lower back, and right hip. A complete blood cell count showed white blood cells 10,900/mm$^3$ (segmented neutrophils 71%, lymphocytes 24%, monocytes 2%, eosinophils 2%, and basophils 1%), hemoglobin 11.9 g/dl, and platelets 230,000/mm$^3$. The Westergren erythrocyte sedimentation rate (ESR) was 65 mm/hr. Rheumatoid factor was negative. Antinuclear antibody was weakly positive at 1:40 dilution. Radiographs of the pelvis and lumbar spine showed bilateral sacroiliitis (Fig. 1) and syndesmophytes. An HLA-B27 test was positive.

Fenoprofen 600 mg tid and sulfasalazine 0.5g bid were prescribed, which led to gradual improvement of the arthralgia. In March 1997, her neck pain worsened with a Westergren ESR of 83 mm/hr. Fenoprofen was replaced by indomethacin. She remained relatively well until July 1997 when she developed a visual disturbance in the left eye. She visited a private ophthalmology clinic, where a visual field examination revealed a defect in inferior altitudinal visual field. This visual deficit improved slowly and spontaneously, but two weeks later she suddenly developed blindness accompanied by severe pain in the right eye, together with frontal headache.

Ophthalmologic examination at our hospital revealed that the visual acuity was finger count in the right eye and 0.8 in the left. There was an afferent pupillary defect in the right eye. The intraocular pressures and slit-lamp examination results were unremarkable in both eyes. The disc was not edematous on ophthalmoscopic examination. The patient's ESR was 52 mm/hr and her C-reactive protein was 0.6 mg/dl (normal < 0.5). Fluorescent angiography showed a faint filling defect around the disc margin in both eyes. A visual evoked potential (VEP) study showed prolonged latency of deflection. Computed tomography and magnetic resonance imaging of the brain were normal.

The patient was admitted to hospital with a diagnosis of optic neuritis and received i.v. methylprednisolone pulse therapy (1 g/day)

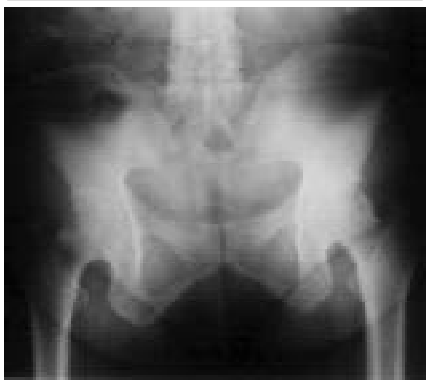

**Fig. 1.** AP view of the pelvis shows bilateral sacroiliitis.