cell count was 12,100/mm³, the haemoglobin concentration was 9.4 g/dl, the haematocrit was 29.1%, the platelet count was 494,000/mm³ and the C-reactive protein was 141 mg/l. Gastroscopy, colonoscopy and CT scanning showed no abnormalities.

For further evaluation, the patient was admitted for [18F]FDG-PET, which clearly demonstrated pathologically elevated glucose uptake within the vessel wall of the whole aorta (Fig. 1A, arrow) and its main thoracic and abdominal branches. The diagnosis of large-vessel vasculitis was subsequently confirmed by the finding of giant cell infiltration (Fig. 1B, arrow) with thickening of all temporal artery layers and consecutive stenosis of the lumen. The patient was treated with prednisone and recovery was unremarkable.

Due to its high sensitivity, especially in the state of active inflammation [1], [18F]FDG-PET might become a valuable diagnostic tool in the management of large-vessel inflammation.

The authors have declared no conflicts of interest.

Correspondence to: M. A. Walter, Institute of Nuclear Medicine, University Hospital, Petersgraben 4, CH-4031 Basel, Switzerland. E-mail: m.a.walter@gmx.net


Rheumatology 2005;44:691–693
doi:10.1093/rheumatology/keh556
Advance Access publication 3 February 2005

Congenital heart block associated with a maternal anti-HsEg5-like autoantibody

Sir, Congenital heart block (CHB) is a rare (1:20,000) disease, and in 70% of cases there are no coexisting cardiac malformations [1]. In this subsect, up to 90% [2, 3] are associated with, if not directly caused by, maternal autoantibodies (Abs) against SSA/SSB (cardiac manifestation of neonatal lupus erythematosus), independently of whether maternal SLE or SS is manifested. Via active placental transfer (increasing after 16 weeks’ gestation), IgG antibodies (Abs) gain access to the fetal heart during a vulnerable phase (from week 16 until shortly after birth), when the main cardiac development is complete and physiological apoptotic

FIG. 1. Continued. Histological confirmation of giant cell arteritis, by finding of giant cell infiltration (arrow) with thickening of all temporal artery layers and consecutive stenosis of the lumen.
events prevail. Damage to the electroconducting system can progress through various stages up to the complete atrioventricular block [4], which carries high mortality (20%) and high morbidity with the need for lifelong pacing (64%) [2].

Less is known about uncommon CHBs in structurally normal hearts without detectable SSA/SSB Abs. We report on such a case associated with an HsEg5-like Ab, being aware that a causal coincidence may not be conclusive.

The 23-yr-old symptomless woman had delivered a healthy child 2 yr ago. In week 21 of her index pregnancy, normal fetal cardiac structures and functions were documented by ultrasound, but in week 35 fetal bradycardia and arrhythmia prompted her admission to our obstetric department, where a second-degree CHB was diagnosed. ANA identified by indirect immunofluorescence on HEp2 cells was positive at 1:640 but without anti-SSA/SSB reactivity [assayed by Varelisa SSA/Ro and SSB/La (Pharmacia & Upjohn Diagnostics, Freiburg, Germany), Line Immuno Assays (Innogenetics, Ghent, Belgium) and western blots of SSA immunoprecipitated from HeLa cell lysates with a commercial anti-52-kDa SSA Ab (Fig. 1A)]. Instead, ANA specificity was found to be directed to a mitotic apparatus (MA) protein as outlined below. Further testing revealed only auto-antibodies against smooth muscle (1:320).

At week 38, a boy (3270 g, Apgar score 5/6/6/8, antibody profile identical to the mother’s) was born spontaneously. Transient sinus node dysfunction and a first- to second-degree alternating CHB with reiterated progression to a third-degree CHB, associated with fatigue, necessitated pacemaker implantation at postnatal day 28.

Notably, the patient’s family had a history of CHBs with need for permanent pacing in 2/5 children of a male third-grade relative.

Among MA proteins, NuMA and HsEg5 have been extensively characterized and described as autoantigens [5–7]. By indirect immunofluorescence, our patient’s MA Ab could not be classified unambiguously. Metaphase cells (Fig. 1B) displayed a bright, crescent spindle pole fluorescence (typical of both NuMA and HsEg5) with staining of spindle fibres in proximity to the poles. HsEg5-typical anaphase interzone spindles did not fluoresce, while postmitotic intercellular bridges did (Fig. 1C). The weak interphase nucleus staining (Fig. 1D) was both diffuse (typical of NuMA) and faintly nucleolar.

On western blots (Fig. 1E) of HeLa lysates from asynchronously growing cells (lane 1) and nocodazole-arrested mitotic cells (lane 2), the maternal Ab(s) recognized ~120-kDa and ~130-kDa proteins respectively (each typical of HsEg5), while showing no reactivity with the 238-kDa NuMA (lanes 3 and 4, probed with a reference anti-NuMA IgM). Because of the lack of commercial reference anti-HsEg5 Abs or recombinant HsEg5, our results could only be compared with, and confirmed by, hitherto published findings: a predicted 116-kDa molecular mass of cloned HsEg5 [6], an 116-kDa HeLa protein (of unsynchronized, predominantly interphase cells) immunoprecipitated by anti-HsEg5 sera [5] and retarded electrophoretic mobility (at 130 kDa) of mitotic HeLa proteins [6], corresponding to metaphase phosphorylated HsEg5 [7].

Additional ~90-kDa immunoreactive bands (Fig. 1E, lane 1) may represent HsEg5 degradation products and/or other auto-antigens. Abs to 90-kDa ASE-1, found to co-occur with anti-HsEg5 Abs [8], seem to be of interest.

Looking for HsEg5 Abs in two other (SSA/SSB Ab-positive) CHB-affected pregnant women, we could not find any reactivity by immunofluorescence or immunoblotting.

Fig. 1. Western blots (A) of SSA immunoprecipitated from HeLa cell extracts by a rabbit anti-52-kDa SSA/Ro antibody (Santa Cruz Biotechnology, Heidelberg, Germany), separated by 12% SDS–PAGE, and probed with our patient’s serum (lane 1), an SSA Ab-positive control serum of a CHB-affected pregnant woman (lane 2), or an ANA-negative control serum (lane 3), each diluted 1:100. Immunofluorescence pattern of our patient’s serum on HEp-2 cells, (B) at metaphase with staining of crescent spindle poles and proximal spindle fibres, (C) at telophase with staining of the intercellular bridge, and (D) at interphase with faintly diffuse nuclear staining; serum dilution 1:40 (B and C) or 1:20 (D). Western blots (E) of extracts from asynchronously growing (lanes 1 and 3) and metaphase-synchronized (lanes 2 and 4) HeLa cells, separated by 6% SDS–PAGE, and probed with our patient’s serum, diluted 1:100 (lanes 1 and 2) or with a monoclonal anti-NuMA Ab (BD Biosciences, Heidelberg, Germany), diluted 1:500 (lanes 3 and 4).
Alternative or multiple pathways seem possible in the pathogenesis of this uncommon CHB. First, genetic conduction diseases (caused by e.g. cardiac channel or transcription factor NKX2.5 gene mutations [9]) might escape detection by ultrasound if they are not associated with cardiac malformations. Further, SSA/SSB Abs levels might be too low to be detected (even by the more sensitive tests), but high enough to be absorbed by the fetal cardiac tissue. In one report [3], the number of 7/67 Ab-negative sera declined to 3/67 on retesting. Finally, Abs other than anti-SSA/SSB, as anti-HsEg5, might also have a pathogenic role; this remains to be clarified.

HsEg5, a kinesin-like microtubule protein, is essential for centrosome separation, mitotic spindle formation [7] and the postmitotic organization of centrosomes and Golgi complexes [10]. Anti-HsEg5 Ab microinjection caused mitotic arrest with growth inhibition [7, 10], and novel antimitic cancer therapies are now targeting HsEg5 [11]. Data on the possible involvement of HsEg5/anti-HsEg5 in mitotic and apoptotic processes during cardiac ontogeny are lacking. To interfere with physiological HsEg5 functions or to evoke inflammation, the maternal Ab must gain access to its cognate antigen. Yet, unlike SSA/SSB [2], the accessibility of HsEg5 in/on normal and pathological tissues (facilitated by proteolytic cleavage) has not yet been demonstrated. But some analogies seem noteworthy in the context of neonatal lupus: like 52-kDa SSA, HsEg5 possesses a coiled-coil domain to which HsEg5 Abs are directed, and HsEg5 Abs, in turn, have been found most often in SLE patients [6].

This paper conforms to standards of the ethical committee of the University of Rostock.

<table>
<thead>
<tr>
<th>Rheumatology</th>
<th>Key message</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• A congenital heart block, outstandingly neither linked to coexisting structural heart anomalies or detectable SSA/SSB Abs, was found associated with an HsEg5-like Ab.</td>
</tr>
</tbody>
</table>

The authors have declared no conflicts of interest.


Departments of Immunology, Obstetrics and Gynecology, University of Rostock, Rostock, Germany

Accepted 24 December 2004

Correspondence to: R. Claus, Institute of Immunology, University of Rostock, Schillingallee 70, 18057 Rostock, Germany. E-mail: renate.claus@med.uni-rostock.de


Rheumatology 2005;44:693–695
doi:10.1093/rheumatology/keh560
Advance Access publication 3 February 2005

**Devic’s syndrome in systemic lupus erythematosus and probable antiphospholipid syndrome**

Neuropsychiatric lupus is common and results in significant morbidity [1, 2]. Antiphospholipid antibodies (aPL) may play a major role and are associated with transverse myelitis [2–4], often with a significant response to anticoagulation [4, 5]. Devic’s syndrome is described in multiple sclerosis (MS) [6] and has rarely been associated with systemic lupus erythematosus (SLE) [5, 7–9]. We present a 44-yr-old woman with SLE who developed neuromyelitis optica and probable antiphospholipid syndrome (APS).

She was healthy until 1990 when schizophrenia was diagnosed. Two years later, SLE was diagnosed based on arthalgias, malar rash, photosensitivity, thrombocytopenia and positive antinuclear (ANA) and anti-DNA antibodies. She remained in remission on corticosteroids but developed diabetes mellitus, hypertension, hyperlipidaemia and osteoporosis. Her aPL had always been negative; she had a previous non-complicated pregnancy and no miscarriages or thrombosis.

In 2003, pulmonary tuberculosis was diagnosed and standard therapy was started but the patient was later switched to rifampicin, pyrazinamide and streptomycin, following a Stevens–Johnson reaction to isoniazid. Immunological markers substantially increased (anti-DNA 1/1280) and anti-histone antibodies were detected. Proteinuria (2.6 g/day), leucocyturia and renal failure (creatinine clearance 14 ml/min) were documented 2 months later and nephritis WHO class IV was diagnosed. She was successfully treated with intravenous (i.v.) cyclophosphamide 1 g/m² and prednisolone 1.5 mg/kg/day.

She was well until the current admission, when she suddenly lost right eye vision and progressively developed bilateral paraesthesiae, lower extremity weakness, right hemiparesis and left arm monoparesis. She was oriented, apyrexial, normotensive and aPL negative; she had a previous non-complicated pregnancy and no miscarriages or thrombosis. She was well until the current admission, when she suddenly lost right eye vision and progressively developed bilateral paraesthesiae, lower extremity weakness, right hemiparesis and left arm monoparesis. She was oriented, apyrexial, normotensive and aPL negative; she had a previous non-complicated pregnancy and no miscarriages or thrombosis.

She was well until the current admission, when she suddenly lost right eye vision and progressively developed bilateral paraesthesiae, lower extremity weakness, right hemiparesis and left arm monoparesis. She was oriented, apyrexial, normotensive and aPL negative; she had a previous non-complicated pregnancy and no miscarriages or thrombosis.