Congenital Heart Block in Infants Born to Mothers With SLE: Maternal-Infant Autoantibody Markers and Management Strategy

By Z. Zain, MBBS; A. A. Majid; A. Omar, MBBS; C. S. Khuan, MBBS; and J. Hassan, MBBS

Introduction
The association between maternal systemic lupus erythematosus (SLE) and adverse fetal outcome due to the transplacental transfer of autoantibodies has been widely reported. Congenital heart block is one of the manifestations of neonatal lupus syndrome and is a recognized cause of morbidity and mortality in infants born to mothers with SLE.

Autoantibodies to SSA/Ro and SSB/La ribonucleoproteins have been demonstrated almost universally in the maternal circulation when isolated congenital heart block is identified [1]. These are soluble nuclear (SSA/Ro) and soluble cytoplasmic (SSB/La) autoantibodies which are directed against cellular ribonucleoprotein complexes predominantly found in patients with sicca syndrome or SLE and is readily identified by the double immunodiffusion method [2].

The presence of these autoantibodies is strongly associated with neonatal lupus, a disorder considered as a model of passively acquired autoimmunity [3]. Complete heart block which is a potentially severe and permanent manifestation of neonatal lupus appearing after the first trimester of pregnancy is an example of this model. The mechanism of disease is dependent on the placental transfer of maternal antibodies (Anti-SSA/SSB) capable of causing specific myocardial inflammation that permanently damages the conduction system of the developing fetal heart [4].

We describe the management and outcome of congenital heart block in infants of mothers with SLE and the association of maternal-infant lupus autoantibody markers.

Patients and Methods
All study infants were born in the single centre in which the study was reported. All infants were identified during fetal ultrasound screening for pregnant mothers with SLE between August 1999 till March 2002.

Connective tissue disease screening including lupus autoantibodies in mothers were examined during antenatal check and the extracted nuclear antigen (ENA) screen was performed for positive serum.

Fetal echocardiography was performed periodically and standard views were obtained to identify structure and intracardiac connections. Fetal M-mode tracings were recorded to determine atrio-ventricular dissociation and estimate left ventricular contractility.

All pregnancies were seen up till term gestation and delivery was planned with the cardiologist and cardiac surgeon on standby.

Infants born were seen immediately by the cardiologists for cardiac assessment. Blood samples were obtained for ANA and specific nuclear antigens.

Results
There were eight patients in this study. There were seven girls and one boy. All patients were diagnosed at the mean gestational age of 28 weeks. Fetal echocardiogram showed normal intra-cardiac structures in all patients with bradydysrhythmia, dilated and moderate to poorly contracting ventricles in seven patients. Fetal cardiac M-mode recorded complete AV dissociation in these seven patients with mild to moderate degree of pericardial effusion. No treatment in-utero was given.

In one patient, the fetal bradycardia was detected during routine ultrasound on the mother and investigations revealed that she was positive for SLE autoantibodies including anti-Ro/SSA despite not being having
performed with the umbilical cord unclamped and placenta not separated until the wires were secured and external pacemaker connected. Patients were then managed in the hospital and permanent pacemaker insertion was performed electively. The median time of permanent pacemaker implantation (n=6) was 30 days (range 18-180 days).

The implantable pacemakers used in all patients were from St Jude’s Medical (Models Microny™ K SR, Microny™ SR+ or Microny™ II SR+) all of which are designed to be used in small patients who needs high base rate pacing (12.8grams, 5.9cc and 6mm thin).

One patient with complete AV block had complete spontaneous recovery to sinus rhythm without treatment. She remains well on follow-up. Two patients died. One patient with a fixed junctional rhythm died of hematological complications related to SLE soon after birth. Another patient died after pacemaker insertion due to respiratory complications at the age of 2 months.

Lupus Autoantibody Profile
All mothers (n = 8, 100%), had ANA positive. Seven (87.5%) of the babies had evidence of transplacental transfer of lupus autoantibodies in which 6 (75%) mother-baby pairs were positive for the anti-SSA/Ro and anti-SSB/La (Table 1). Two babies were strongly positive for ANA (> 1:1000), 3 had in addition anti-sm/RNP, anti-cardiolipin 7 and anti-Jo1 positive respectively.

Period of follow-up is between 1-3 years. All patients with pacemakers are thriving well with satisfactory normal left ventricular dimensions and function on echocardiogram. None of the patients are on any cardiac medications. The outcome of patients in this study is shown in Figure 1.

Discussion
Neonatal lupus is characterized by cutaneous lesions, heart block or both [2]. The type of in-utero heart blocks reported range from partial to complete atioventricular block and is due to fibrosis of the conduction system. Antenatal detection has allowed peripartum management including use of beta-agonists and steroids but the mainstay of treatment remains the insertion of single chamber ventricular pacemaker.

Mothers with SLE are at risk to bear children with congenital heart block. The overall risk of giving birth to an infant with congenital heart block, among women with probable or definite SLE was 1:60 but when the woman had anti-SSA/Ro, the risk was 1:20 [5].

In this study, all infants were detected during routine ultrasound check for women with SLE who were pregnant.

“Congenital heart block is one of the manifestations of neonatal lupus syndrome and is a recognized cause of morbidity and mortality in infants born to mothers with SLE.”
These patients were then carefully followed up till term gestation with pre-existing management plans in order for the infant with congenital heart block except for one. In one patient, the mother had clinical features of SLE including hematological disease and died post-partum secondary to disseminated intravascular coagulation (DIVC). The baby had a fixed junctional type of heart block of 60 beats per minute despite intravenous infusion of isoprenaline and succumbed rapidly due to severe hematological abnormalities. No pacemaker insertion was attempted.

All babies with decompensated complete AV block (n=6) had an external temporary pacemaker with epicardial wires inserted to the right ventricle by thoracotomy soon after birth. Cardiac decompensation was determined clinically as the presence of signs of poor cardiac output. Two newborns had their procedure done on a side table to the mothers with the umbilical cord unclamped with the placenta intact in the uterus as soon as the baby was delivered by caesarean section. The patent flow across the umbilical vessels provided adequate volume and stimulation and both procedures were completed without any complications.

Permanent subcutaneous implantable pacemakers (single chamber) with bipolar steroid eluding epicardial leads were electively inserted in six patients. The optimal time for permanent pacemaker insertion was determined by the weight of the baby and this was achieved by establishing adequate nutrition and treating concurrent infections.

Previous management experience in our institution before this study for a small number of babies with similar history were not satisfactory. Transvenous pacemaker wire was inserted either by the femoral vein or umbilical vein route while awaiting permanent pacemaker insertion which was complicated by infection at the insertion site or recurrent dislodgment of the lead wire.

Patients weighing or had achieved weights of 3.2 Kg and above were scheduled for permanent pacemaker insertion. Pacemaker implantation was done in a subcutaneous pocket created in the subcostal region in all patients and epicardial leads secured to the epicardium adjacent to the right ventricle and allowing excess wire to allow for growth and movement. We found this strategy of staged approach to have good outcome albeit longer stay for the patient in hospital.

<table>
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<th>Baby anti-Ro/ anti-La</th>
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<td>Pos / Pos</td>
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</tr>
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<td>Pos / Neg</td>
<td>Pos / Pos</td>
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<tr>
<td>8</td>
<td>Positive</td>
<td>Pos / Pos</td>
<td>Pos / Pos</td>
<td>Junctional Heart Block</td>
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</table>

Table 1. Maternal-infant lupus autoantibody profile

The experience with the existing patients in this study has allowed us to organize a multi-disciplinary approach in the management of these infants beginning from ante-natal period in which pregnant mothers are counseled by the rheumatologists and obstetricians. Upon detection of any cardiac abnormalities particularly heart block, the pediatric cardiologists and cardiac surgeons are then involved in the planning of the post-natal management of these infants.

Perinatal treatment has not been proven to be useful to improve heart rate or ventricular contractility except for experiences in small numbers of patients [14-17] and therefore not practiced in our center. Steroids are used, however, to expedite lung maturity if necessary.

Permanent pacemaker insertion is the definitive treatment for babies with congenital complete AV block and the ideal situation would be to be able to manage them through perinatal period and achieve a safe delivery.

Miniaturized permanent pacemakers in this current era has allowed early insertion and eliminated the issue of the infant’s size and weight for selected centers.

We have adopted the staged approach for pacemaker insertion in our infants in view of our limitations and this strategy has shown to have good outcome.
Conclusion

Congenital heart block is a rare but serious fetal adverse disease due to maternal-fetal transmission of anti-SSA/Ro in pregnant mothers with SLE. Anticipation of this condition and early detection by fetal echocardiography allows an organized multi-disciplinary management with a staged approach which promises favorable results.

References

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