

**NEONATAL LUPUS SYNDROME: THE ROLE OF MATERNAL
SS-A(RO) AND SS-B(LA) ANTIBODIES
A CASE REPORT**

Reda Ali Ebrahim, MRCPUK)* Anil Kumar Chawla, MD**

A patient, who developed systemic lupus erythematosus (SLE) five years after she gave birth to a daughter with congenital heart block, is presented. She was clinically normal at the time of that delivery. Her immunological investigations revealed antibodies against SS-A (Ro) and SS-B (La) antigens. The aspects of latency until the development of clinical SLE, the role of such maternal antibodies in the development of fetal congenital heart block and the possibility of its prevention, using Dexamethasone and plasmapheresis during pregnancy are discussed. Bahrain Med Bull 1995;17:

Women with systemic lupus erythematosus (SLE) have a higher frequency of miscarriage, intrauterine growth retardation, still birth and premature delivery. However 70-80% of SLE pregnancies result in a live birth. In some instances the pregnancy continues until full term but the infant is born with bradycardia due to conduction system abnormalities. The congenital heart block, in addition to cutaneous lupus lesions and some hematological abnormalities are together termed Neonatal Lupus Erythematosus (NLE) and were described by Hull et al in 1966.

Later work has shown a strong association between maternal SS-A(Ro) and SS-B(La) antibodies and the Neonatal Lupus Syndrome². We report here a patient in whom SS-A(Ro), SS-B(La) antibody positive SLE was diagnosed five years after she gave birth to a daughter with the congenital complete heart block and at which time she was completely asymptomatic. We believe that this is the first such reported case in Bahrain.

THE CASE

HAF, a thirty one year old Egyptian housewife, was referred from the Primary Health Centre to the Skamania Medical Centre for the investigations of pyrexia of unknown origin.

* Consultant Physician & Rheumatologist
** Medical Doctor
Department of Internal Medicine
Salmaniyah Medical Centre
State of Bahrain

Patient gave two years history of intermittent pain and swelling of the joints of hands, feet, shoulder, neck, knees and ankles. There was a history of early morning stiffness lasting two to three hours. The pain responded partially to non steroidal anti inflammatory drugs. Two months prior to admission she had been running a moderate grade fever without much joint pains or swelling. There was no history of skin rash, Raynaud's phenomena, cardiorespiratory or abdominal symptoms. She complained of loss of hair from her scalp.

The patient had two daughters, the elder twelve and the younger affected with neonatal lupus, nine years old. She had an abortion at four months gestation in 1989, and has secondary infertility since then.

Her younger daughter who is suffering from neonatal lupus was born on July 1985 at full term through a Caesarean section done because of a cephalopelvic disproportion. She was unwell soon after birth with cough and nasal discharge.

The first ECG of the daughter done at three months of age revealed a complete heart block (CHB) with a ventricular rate of 65 per minute and normal QRS complexes (Fig 1). An ECG done in December 1994 showed similar changes. Echocardiography did not reveal any structural cardiac abnormality. She remained asymptomatic, her milestones were normal, and she grew up normally.

Her heart block, though persistent did not require a pacemaker because of an adequate spontaneous ventricular rate. At the time of birth of this daughter in 1985 our patient was completely asymptomatic. No investigations were done to her during pregnancy or later until she presented with fever in September 1990.

On examination in September 1990, the patient had a fever of 37.60C, and two small firm lymph nodes in her right axilla. There was evidence of synovitis of wrists, metacarpo-phalangeal, metatarsophalangeal and ankle joints. There was restriction of movements of neck, shoulders and knees due to pain. Hip joints were normal. Rest of the systemic examination was unremarkable.

Laboratory investigations: Hemoglobin 10.1 gm%, platelets count 118000/c.mm, white blood cells 4200/c.mm, polymorphs 50%, lymphocytes 36%, eosinophils 10%, and myelocytes 4%. ESR 90 mm 1st hour Westergren. C-Reactive Protein positive. X-Rays of the hands only showed soft tissue swelling of PIP joints. X-Ray chest normal. Liver function tests showed reversal of A:G ratio but otherwise normal. Renal function tests including 24 hours protein and creatinine clearance normal. Thyroid functions normal. Lymph node biopsy showed reactive hyperplasia and bone-marrow aspiration was normal. Immunological work-up revealed Anti Nuclear antibodies positive, titer 1:40,000 (Speckled pattern). Anti double stranded DNA antibody positive. LE cell phenomenon positive. Rheumatoid factor (Latex Agglutination) negative. Antibodies against extranuclear antigens AA-A(Ro) positive, SS-B(La) positive, SM positive, RNP positive. Immunological work up for the 9 years old daughter with complete heart block revealed. Anti SS-A(Ro), Anti SS-B(La), Anti RNP and Anti SM antibodies were all negative as tested on 1st December 1994. Anti dsDNA negative and ANA negative.

The patient was diagnosed to be suffering from SLE and she was started in corticosteroids on November 1990. She showed a very good response to treatment and for the first time felt better. Azathioprine was added in April 1991 and the dose of prednisolone was reduced. She was maintained on this medication and she remained fairly well controlled.

In February 1994, she developed lupus pneumonitis which responded well to bolus intravenous cyclophosphamide 750 mg every four weeks for six doses. She is presently stable and is maintained on Prednisolone 5 mg daily.

DISCUSSION

It is well recognized that the birth of a baby with complete heart block may predate the development of connective tissue disease in the mother by many years³.

Up to 70% of mothers of infants with NLE are symptom free at the time of delivery and are identified only by the birth of an affected child, and so cannot be identified prospectively⁴. It is on follow-up that up to two thirds of the affected infant's mothers show laboratory or clinical evidence of SLE or other connective tissue disease. We do not know however, if these mothers are also immunologically and biochemically normal at the time of delivery of the

affected baby. Only a prospective study could establish that. And even if an immunological abnormality is found at the time of delivery or soon after, what is the reason for such a long latency until the development of a clinical connective tissue disorder?

Such apparently unaffected mothers of infants with congenital heart block need close follow-up, not only for the development of connective tissue disease later in life but also because the risk of NLE in a subsequent child may be as high as 1 in 4⁵ and preventive treatment if applied early in pregnancy may be useful.

There is a strong association between the presence of SS-A(Ro) and SS-B(La) antibodies in the mother and the affected infant with congenital heart block³. SS-A(Ro) antibodies are found in approximately 25% of patients with SLE in general and their presence in infants with isolated congenital heart block is almost universal⁶.

The incidence of congenital heart block is one in 20,000 live births in general. The risk of having an infant with congenital heart block is not established in women who are known to have SLE and the high estimates of 1 in 60 in all SLE pregnancies and 1 in 20 in mothers with anti-Ro antibodies have been disputed⁷.

Although heart block is present at birth, the cutaneous lupus lesions may appear in the first two months and resolve by six months and hematological abnormalities like thrombocytopenia, autoimmune hemolytic anemia and raised liver enzymes may be variably present.

The cause of neonatal lupus syndrome, particularly the congenital heart block is the passive transplacental transfer of maternal IgG antibodies against the SS-A and SS-B antigens. At 18-24 weeks of fetal life high levels of SS-A antigens have been demonstrated in fetal cardiac tissues. The autoimmune reaction in the cardiac tissue leads to inflammatory myocarditis with extensive endocardial fibroelastosis and replacement of the atrial septum and the AV node by elastic and fibrous tissue⁸.

The appearance of the disease in the neonate coincides with the presence of maternal antibodies in the fetal and neonatal circulation, and except for cardiac abnormalities, the disease resolves with the clearance of the maternal antibodies by the eighth month of postnatal life⁹. This explains why the daughter of the patient tested negative for such antibodies at the age of nine years.

About 25% of NLE infants with congenital heart block may have associated structural congenital heart defects¹¹. Many, though not all infants with congenital heart block require a permanent pacemaker⁵. Some of these infants with NLE may develop adult onset connective tissue disorder later and this may only reflect an increased genetic predisposition¹¹.

Attempts to prevent the development of cardiac lesions have been made with some success, using prophylactic dexamethasone treatment and plasmapheresis to lower maternal Ro antibody titers¹⁰. Pregnant women at high risk are those with known connective tissue disease, high titers of SS-A and SS-B antibodies, previous children with congenital heart block, and genetic predisposition with HLA-DR3, which occurs in most mothers of NLE infants. Such women need to be monitored closely during pregnancy for the early detection of fetal bradycardia and heart defects with fetal echocardiography⁸.

CONCLUSION

Neonatal Lupus Syndrome should be considered in any child born with bradycardia or congenital heart block. The mother and the child should be investigated for

the presence of SS-A(Ro) and SS-B(La) antibodies in their sera. The mother should be followed up for the possible development of collagen disease and the future pregnancy should also be closely monitored with fetal echocardiography for early detection of heart blocks or structural heart defects in the foetus. If such abnormalities are detected, treatment with dexamethasone and/or plasmapheresis is found to be helpful in improving the outcome in a small number of reported cases.

REFERENCES

1. Hull D, Binns BAO, Joyce D. Congenital heart block and widespread fibrosis due to maternal lupus erythematosus. Arch Dis Child 1966;41:688-90.
2. Watson RM, Lane AT, Barnett NK, et al. Neonatal lupus erythematosus. A clinical, serological and immunogenetic study with review of the literature. Medicine 1984;63:362-78.
3. Fox R, Sharp D, Evans I. Systemic lupus erythematosus in pregnancy. Lancet 1991;338:87-8.
4. Lockshin MD, Bonfa E, Elkouf K, et al. Neonatal lupus risk to newborns of mothers with SLE. Arthritis Rheum 1988;31:697-701.
5. McCune AB, Weston WL, Lee LA. Maternal and fetal outcome in neonatal lupus erythematosus. Ann Intern Med 1987;106:518-23.
6. Provost TT, Watson R, Gammon ER, et al. The neonatal lupus syndrome associated with anti-RNP (nRNP) antibodies. N Engl J Med 1987;316:1135-8.
7. Brucato A, Ferraro G, Gasparini M. Congenital heart block and maternal SLE. Lancet 1991;338:892.
8. Muller-Ladner U, Benning K, Rother E, et al. Neonatal lupus syndrome as an example of passively acquired autoimmunity. Immun Infekt 1992;20:117-21.
9. Buyon JP, Winchester R. Congenital complete heart block. Arthritis Rheum 1990;33:609-14.
10. Bierman FZ, Baxi L, Jaffe I, et al. Fetal hydrops and congenital complete heart block: response to maternal steroid. J Pediatr 1988;119:646-58.
11. Esscher E, Scott JS. Congenital heart block and maternal systemic lupus erythematosus. Br Med J 1979;i:1235-8.