Pregnant women with autoantibodies to Ro/SSA and/or La/SSB have an increased risk to give birth to children with atrioventricular block (AV block). This condition is part of the neonatal lupus syndrome that may also include skin, liver, or hematological abnormalities and that depends on transplacentally transferred pathogenic maternal autoantibodies. The exact risk percentages are difficult to calculate correctly, as the mothers may be completely asymptomatic. In pregnancies succeeding one complicated by fetal AV block, the risk for the same conduction disturbance is 8–16%. Mothers with diagnosed connective tissue diseases (CTD) and babies with AV block often have primary Sjögren’s syndrome (SS) with its characteristic autoantibody profile and genetic background rather than features of systemic lupus erythematosus. In a study of Danish and Swedish patients with SS the risk of congenital AV block was increased 500-fold. Current opinion is that established third-degree AV block is irreversible and not successfully treatable. Careful monitoring and dexamethasone treatment when first signs of cardiac dysfunction without block appear has been proposed and shown to be effective in one case. A recent retrospective study has shown that dexamethasone might improve the outcome of the pregnancy compared with untreated fetuses. In 4 cases second-degree AV block resolved into a first-degree block at birth.

We describe a further case of successful management of intrauterine second-degree AV block in a fetus of a patient with primary SS with high disease activity and anti-Ro (60 kDa and 52 kDa) and anti-La autoantibodies.

CASE REPORT

Our patient was a 31-year-old woman. At age 17 years she had developed Waldenström hyperglobulinemic purpura and some years later dry eyes, dry mouth, fatigue, and photosensitivity. Arthralgias, arthritis, diffuse hair loss, fever, and finally severe dyspnea due to interstitial lymphocytic pulmonary infiltration developed. No kidney manifestations occurred at any time. She had earlier low leukocyte and lymphocyte counts, high plasma IgG levels (58.5 g/l), high antinuclear antibody titer (16,384, HEp-2), positive anti-Ro/SSA and anti-La/SSB antibodies, transiently weakly positive anti-dsDNA antibodies, and positive IgM rheumatoid factor. Low levels of C3 and C4 complement factors and anti-C1Q antibodies were found in ELISA. Six objective tests for ocular and oral glandular function were pathological.

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She fulfilled the Copenhagen and European classification criteria for primary SS; the Fox/Saito criteria were not applicable since a salivary gland biopsy was never performed. Her brother had undifferentiated CTD with arthritis, hemolytic anemia, and Libman-Sacks endocarditis.

Because of her severe pulmonary disease she had been treated with prednisolone and cyclosporine since 1995, with varying dosage depending on disease activity. This treatment was continued during conception and pregnancy because of severe relapses during attempts to further reduce the cyclosporine dosage. During early pregnancy the cyclosporine dosage was 3 mg/kg/day. No plasma concentration measurement was done. The prednisolone dose was 10 mg per day.

**Pregnancy.** The initial phase of the pregnancy was uncomplicated. The patient was treated with 75 mg acetylsalicylic acid in addition to prednisolone and cyclosporine in order to minimize thrombosis within the uteroplacental circulation. She was informed about the risk of fetal heart block and was followed closely. Completely normal heart rate and anatomy was recorded at week 17 + 1. At week 19 + 0 the midwife observed intermittent fetal bradycardia and this was confirmed by sonography. Later the same day the fetal heart rate was constantly reduced to 69 beats per minute (bpm). The situation was initially interpreted as an AV block III. Retrospectively a revision of the fetal echocardiography tapes showed a 2:1 atrial/ventricular rate (atrial rate 138 bpm, ventricular rate 69 bpm). Venous Doppler blood velocity pattern indicated second-degree AV block instead of third-degree at that time. We decided to treat the patient with 4 mg dexamethasone po/day instead of her prednisolone. Dexamethasone is not inactivated by the placenta in contrast to prednisolone, thus making treatment of the fetal tissue with glucocorticosteroids possible.

The situation remained unchanged during the first 3 weeks of treatment, but at week 23 + 6 fetal heart rate improved and now a block of every third atrial beat was recorded. At 24 + 4 weeks only every fourth or fifth ventricular beat was missing and from week 25 + 2 a normal fetal heart rate of about 140 bpm was monitored at all following visits until delivery by cesarean section at week 33 + 3. Figure 1 illustrates the fetal heart rate development from week 19 to 25.

Uterine artery blood velocity showed signs of bilateral diastolic notch, which is associated with perinatal complications such as pregnancy induced hypertension and intrauterine fetal growth restriction. Cardiac anatomy and function were normal. No pericardial or pleural effusions or ascites could be detected. Fetal growth was somewhat retarded, which might be secondary to both the cyclosporine treatment and disturbance in utero-placental blood velocity. No signs of oligohydramnios could be detected.

**Immunological tests.** During pregnancy the mother’s autoantibodies were analyzed by ELISA and immunoblotting and high titers of antibodies against Ro(SSA) 60 kDa, Ro(SSA) 52 kDa, and La(SSB) were found. IgG, IgA, and IgM autoantibodies were all present in the mother’s circulation (IgM only against Ro-52 kDa and La). As expected, the baby’s blood at birth showed only IgG autoantibodies, but as in the mother against all 3 investigated SSA/SSB components (Figure 2).

**Postnatal status.** At birth the baby was well, with a birth weight of 1720 g, which is 30% below the mean normal birth weight for gestational age. The Apgar score was 9-9-10. Transient hypoglycemia, thrombocytopenia, and hyperbilirubinemia treated with phototherapy were observed. All other blood tests were normal. A slight prolongation of the PQ time (first-degree AV block with PQ time 140 ms) was detected. During the followup period of 8 months the AV block persisted unchanged and the baby grew without any further complications (Figure 3). No other manifestations of neonatal lupus were noticed.

**DISCUSSION**

Our case confirms the possibility of successful in utero treatment of incomplete heart block in a fetus with neonatal lupus syndrome by maternal dexamethasone therapy. The patient had an aggressive disease with exocrine and non-exocrine SS and the subspecificities of autoantibodies associated with high risk of congenital heart block. Close monitoring of the fetal heart rate from week 16 allowed us to detect the development of fetal bradycardia and start dexamethasone treatment without delay. The cyclosporine treatment that otherwise had a very good effect on the patient’s severe pneumonitis did not prevent the fetal AV block.

At first appearance of a fetal bradycardia it can be difficult to differentiate between second-degree and complete AV block. There is one case report on the reversal of complete fetal AV block during prednisolone treatment of the mother for a dermatological disorder and some reports about lessening of complete AV block during treatment with fluorinated corticosteroids. But generally, established third-degree block is interpreted as a result of fibrosis of the conduction system and likely to be permanent. However, this should not lead to therapeutic nihilism in any recent onset congenital AV block. Instead, in agreement with recent suggestions, we would recommend treatment of all newly detected cases of AV block without delay, thus avoiding missing the chance to prevent progression from second to third-degree at that time. We decided to treat the patient with 4 mg dexamethasone po/day instead of her prednisolone. Dexamethasone is not inactivated by the placenta in contrast to prednisolone, thus making treatment of the fetal tissue with glucocorticosteroids possible.

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third-degree block or the possibility to successfully reverse the inflammatory process in the conduction system. Possibly all complete blocks develop via a period of instability with first-degree and/or second-degree AV block. In these cases close monitoring of fetal heart rate during the critical period of pregnancy may enable early treatment of the pathogenic process, with reduced morbidity and mortality as a possible result.

REFERENCES


Figure 2. IgG autoantibody profiles of a mother with primary SS and her child with fetal AV block, analyzed by ELISA (performed as described").

Figure 3. The child’s postnatal electrocardiogram, showing AV block I. PQ time 140 ms. Heart rate 147 bpm.


