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RESEARCH ARTICLE

ANTENATAL DIAGNOSIS OF FETAL HEART RHYTHM DISORDERS IN WOMEN WITH LUPUS WITH POSITIVE ANTI-SSA AND ANTI-SSB ANTIBODIES: ABOUT TWO CASES

Ibtissam Bellajdel, Hind Bouyabla*, Benhamou Imane, Hafsa Taheri, Hanane Saadi and Ahmed Mimouni
Department of Gynecology and Obstetrics, Mohammed VI-Oujda University Hospital, faculty of Medicine and Pharmacy, Mohammed Premier University, Oujda, Morocco.

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Abstract

Lupus erythematosus is a nonorgan-specific autoimmune disease predominantly affecting young women of childbearing age, as well as neonatal lupus is a complication related to the presence of anti-SSA/Ro or anti-SSb/La antibodies in the mother. Cardiac manifestations of neonatal lupus include anti-SSA/Ro-SSB/La-mediated conduction system disease and endocardial/myocardial damage resulting in cardiomyopathy. Pregnancy is a complicating factor in lupus erythematosus in 60% of cases. These complications do not seem to be related to the number of pregnancies or to the duration of remission, but stopping the hydroxychloroquine treatment could be the cause of relapses. Obstetrical complications due to lupus are dominated by intrauterine growth retardation and prematurity in 30% of cases, abortion or fetal death in utero in 20% of cases, especially in the presence of anti-phospholipid antibodies and/or anti-cardiolipin antibodies in the mother, and complete atrioventricular block in 1.6% of cases due to trans-placental passage of anti-SSA antibodies. Some treatments, including hydroxychloroquine, corticosteroids, and certain immunosuppressants (azathioprine) are safe, and can and should be maintained if necessary during pregnancy.

Introduction:-

Neonatal lupus erythematosus (NLE) is a rare autoimmune disease due to transplacental passage of maternal autoantibodies (1) across the placental barrier by a mother with autoimmune disease (2). It is certain that these autoantibodies, especially those directed against soluble core antigens, called SSA/Ro and SSB/La, correlate with clinical manifestations. The term neonatal lupus is actually misleading since most mothers do not have systemic lupus erythematosus (SLE) but other autoimmune diseases such as Sjogren's syndrome (SS) or undifferentiated connective tissue diseases or no clinically proven pathology(1). The most important clinical manifestation of neonatal lupus is congenital atrioventricular block (cAVB), which is most often complete (i.e., 3 rd degree) (1), occurring on a heart free of malformative heart disease, dilated cardiomyopathy, and endocardial fibroelastosis (3). The cutaneous and systemic attacks are transient, contrary to the congenital atrioventricular block which is definitive and associated with a morbidity and a mortality which make all the gravity of this syndrome (4, 5, 6).from where the interest of the antenatal diagnosis of the cardiac demonstrations to ensure better ante- and neonatal management.

Corresponding Author:- Hind Bouyabla
Address:- Department of Gynecology and Obstetrics, Mohammed VI-Oujda University Hospital, Faculty of Medicine and Pharmacy, Mohammed Premier University, Oujda, Morocco.

We report in this document, observation of 2 patients, in whom the diagnosis of neonatal lupus erythematosus was retained with positive antibodies anti SSA and anti SSB.

Observations:-

Case1:

Mrs A.K. 31 years old, Gestity 2 Parity 2 (Gestity n 1: full term pregnancy, vaginal delivery of a male newborn, currently 4 years old, Gestity n 2: fetal death in utero at 34 weeks of amenorrhea, Gestity2: current pregnancy estimated at 35 weeks of amenorrhea according to the date of the last menstrual period), followed up for systemic lupus with the following clinical manifestations: non-deforming peripheral polyarthritis affecting small and large joints, a butterfly rash and a nephrotic syndrome with the presence of anti-nuclear antibodies (ANA), anti-native DNA antibodies, anti-SM antibodies, anti-SSA and anti-SSB antibodies in the immunological assessment. A renal biopsy was performed showing a stage IV lupus nephropathy. The search for a secondary antiphospholipid syndrome showed the presence of anti-cardiolipin and anti-BETA2 Glycoprotein (B2GP1) antibodies at low to moderate levels. Obstetrical ultrasound had objectified: progressive mono fetal pregnancy, in cephalic presentation, biparietal diameter at 90 mm, abdominal circumference at 314 mm, femoral length at mm 68 which corresponds to 35 weeks of amenorrhea, estimation of fetal weight at 2kg700, anterofundial placenta, amniotic fluid in normal quantity, with the presence of an auriculoventricular block stage III. The evolution under treatment based on corticoids and azathioprine was favorable on the general level, whears , on the renal and the obstetrical level, they were complicated by the appearance of an auriculoventricular block degree III; an extraction by C-section was performed for fetal rescue, giving birth to a female new born with a weight of birth of 2kg800, she benefited from a echocardiography showing no congenital heart abnormality and no defects, but the electrocardiogram objectified a complete 3rd degree BAV, the new born died within 4 days.

Case 2:

Mrs F.M. Mrs F.M., 29 years old, 4 parity (parity 1: fetal death in utero at 36 weeks of amenorrhea, parity 2: spontaneous miscarriage of 2 months,uncurreted; parity 3: uncurreted spontaneous miscarriage of 3 months, parity 3: current pregnancy estimated at 37SA +4 days according to the date of the last precise menstrual period), followed up for systemic lupus for 2 years under hydroxychloroquine with the following clinical manifestations: non-deforming peripheral polyarthritis affecting the small and large joints and a nephrotic syndrome with the presence of anti-nuclear antibodies (AAN), anti native DNA antibodies, anti Sm, anti SSA and anti SSB antibodies in the immunological assessment. Obstetrical ultrasound had objectified: non evolving mono fetal pregnancy, in cephalic presentation, biparietal diameter at 91 mm, abdominal circumference at 321 mm, femoral length at 74 mm which corresponds to 37 weeks of amenorrhea, estimation of fetal weight at 3kg ,posterofundial placenta, amniotic fluid in normal quantity. The evolution under hydroxychloroquine treatment was favorable on the general basis and on the renal level also, but complicated on the obstetrical level by fetal death in utero; therefore, an induction of laborwas performed giving birth to a stillborn of male sex with a weight of birth of 3kg100.

Discussion:-

Neonatal lupus erythematosus (NLE) is a rare syndrome secondary to transplacental transmission of anti-SSA (Ro) and/or anti-SSB (La) antibodies, starting at 16 weeks of pregnancy and gain fetal tissue. It mainly affects the skin and the heart, but hematological, hepato-biliary and neurological involvement may also be present. Skin involvement may be present at birth or a few weeks later (8). BAVc is the most common cardiac complication of LEN. In contrast to the transient skin involvement of LEN that occurs in the neonatal period, cAVB is most often permanent and occurs in utero, making the term "neonatal lupus" inappropriate. LEN BAVc usually occurs in a heart free of malformative heart disease (9). Most mothers are asymptomatic at the time of LEN diagnosis but have elevated levels of anti-SSA (Ro) and/or anti-SSB (La) antibodies, which are also present in the newborn (1). BAVc is characterized by the presence of immune complex deposits, inflammation, calcifications and fibrosis in the fetal atrioventricular node (8).It is most often discovered between 20 and 24 weeks of amenorrhea (SA), during a routine ultrasound or when fetal bradycardia is found on heart sound auscultation. It is most often an irreversible third-degree BAV; more rarely second- or first-degree [10]. This complete and definitive BAVc is manifested on fetal echography by a complete atrioventricular dissociation (normal atrial rhythm and ventricular rate lower than 100 bpm).it can be a first or second degree BAV, sometimes spontaneously reversible, or on the contrary, evolving and associated with a postnatal progression justifying a systematic regular monitoring (11).Other cardiac conditions that may occur include: 1st or 2nd degree BAVc have been reported in neonates with sometimes postnatal progression of the degree of BAVc [12], warranting routine ECG in children born to mothers with anti-SSA/Ro antibodies;

Corrected QT prolongations and sinus bradycardia of spontaneous resolution in otherwise healthy children born to mothers with anti-SSA/Ro antibodies have been described [13] but remain controversial [14]; Late dilated cardiomyopathies associated with BAVc with a poor prognosis have been reported with an incidence varying from 5 to 11% of BAVc cases [15, 16]. These cardiomyopathies occurred despite early pacemaker implantation in children who had normal ventricular function at birth. Myocardial biopsies have shown myocyte hypertrophy and interstitial fibrosis [15]; and Cases of fibroelastosis without cAVB associated with maternal anti-SSA antibodies have been described [17].The action of the antibodies causes progressive degradation of the nodal tissue leading to fetal atrioventricular block (fAVB) of increasing severity and of more or less rapid onset leading to complete atrioventricular dissociation [18].As in postnatal, fetal atrioventricular blocks are classified into three types according to their severity:
-BAV of degree 1 (BAV1), reported by a fixed and constant prolongation of the fetal atrioventricular conduction time (TAVf).
-BAV of degree 2, the interruption of the atrioventricular conduction is intermittent (Mobitz block type 1 or 2);
-BAV of degree 3 or complete corresponding to a total atrio-ventricular dissociation.

There is then an idioventricular escape rhythm whose frequency differs according to the level of conduction block on the bundle of His.There are four main methods to measure the TAVf.The first one consists in a measurement in time-motion mode (TM) and the three others in pulsed doppler mode.BAVc warrants a dual therapeutic approach: prophylactic and curative (19). Curative treatment involves drugs to accelerate the fetal heart rate, which are moderately effective, and the fluorinated corticosteroids, dexamethasone or betamethasone, which have transplacentalpassage(9). Seven of twenty fetuses (35%) with second-degree BAV exposed to fluorinated corticosteroids had complete regression or progression to first-degree block, compared with 1 of 16 (6.25%, p. = 0.053) for those not receiving corticosteroids [19]. Incomplete BAVc, especially those associated with myocarditis or fibroelastosis are for many authors an indication for fluoride corticosteroids. The management of third-degree BAV is much more controversial. Regression of complete BAVc is rare; only one case of reversion of a BAV has been published [20]. Given the complications associated with the use of corticosteroids during pregnancy (diabetes, hypertension, intrauterine growth retardation, oligohydramnios), many authors advocate therapeutic abstention or a very short treatment. In all cases, specialized obstetrical and cardiopediatric care is essential, with the installation of a pacemaker if necessary. Regular follow-up is essential given the risk of progression of the AVB and the appearance of late cardiomyopathy. As for delivery, a caesarean section is generally scheduled, given the impossibility of detecting fetal distress by monitoring the fetal heart rate during labor(3).Screening for congenital atrioventricular block by monitoring the fetal heart rate between 16 and 24 days of pregnancy, every two weeks, or even every week if there is a history of AVB [21].Since the risk of AVB is 1 to 2% in the presence of an anti-SSA/Ro antibody, no prophylactic treatment is indicated in women without a particular history. However, the risk is higher (16 to 19%) [19-21] in women who have already had a child with AVB and hydroxychloroquine seems to be of interest in this indication [22].In order to diagnose early the occurrence of a first degree AVB, the measurement of the fetal atrioventricular conduction time (fAVC) must be performed regularly during pregnancy.In a review of the literature, Monsarrat et al. control the following monitoring:
-if there is a history of complete BAVf: weekly monitoring of TAVf between 16 and 26 SA;
-in the absence of a history: monitoring of TAVf every 15 days between 16 and 26 days of age.

Conclusion:-

The clinical manifestations of neonatal lupus are polymorphic and the only one that can represent a considerable risk is complete atrioventricular block.Obstetrical ultrasound performed at least every 2 weeks, starting at 16 weeks of gestation, are recommended in anti-Ro/SSA-positive pregnant women: the aim is to detect early fetal abnormalities, which could precede complete atrioventricular block and which could be targets for preventive treatment.

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