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Published in:
Clinical and Experimental Rheumatology

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2021

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

Sjogren Big Data Consortium, Brito-Zeron, P., Pasoto, S. G., Robles-Marhuenda, A., Mandl, T., Vissink, A., Armagan, B., Praprotnik, S., Nocturne, G., Sebastian, A., Fernandes Moca Trevisani, V., Retamozo, S., Acar-Denizli, N., Wiland, P., Siso-Almirall, A., Bootsma, H., Mariette, X., Ramos-Casals, M., & Kostov, B. (2021). Autoimmune congenital heart block and primary Sjogren's syndrome: characterisation and outcomes of 49 cases. *Clinical and Experimental Rheumatology*, 38(4), S95-S102. <https://www.clinexprheumatol.org/abstract.asp?a=16255>

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Autoimmune congenital heart block and primary Sjögren's syndrome: characterisation and outcomes of 49 cases

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Received on August 3, 2020; accepted in
revised form on September 10, 2020.

Clin Exp Rheumatol 2020; 38 (Suppl. 126):
S95-S102.

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EXPERIMENTAL RHEUMATOLOGY 2020.

Key words: autoimmune congenital
heart block, primary Sjögren's
syndrome, neonatal lupus, anti-Ro
antibodies

Competing interests: X. Mariette received
an honorarium for consultancy advice
on Sjögren's syndrome from BMS, GSK,
Novartis and Servier and a research grant
from Servier.
The other authors have declared
no competing interests.

ABSTRACT

Objective. To characterise autoimmune congenital heart block (CHB) associated with a maternal diagnosis of primary Sjögren's syndrome (pSS) confirmed either before, concomitant or after the first pregnancy complicated with CHB.

Methods. The following inclusion criteria were applied: (i) Mothers with positive Ro/La autoantibodies detected previously or at the time of diagnosis of the first case of CHB; (ii) diagnosis of CHB confirmed by fetal echocardiography; (iii) AV block diagnosed in uterus, at birth or within the neonatal period (0-27 days after birth) (8); (iv) absence of anatomical cardiac abnormalities which might be causal of AV block; and (v) maternal fulfillment of the 2002 SS criteria before, during or after having a pregnancy complicated with CHB.

Results. We identified 49 cases of autoimmune CHB in children born from 44 mothers who had a mean age at the time of pregnancy of 30.3 years (range 18 to 41). At the time of diagnosis of autoimmune CHB, all mothers had positive anti-Ro antibodies and 28/44 (64%) were positive for anti-La antibodies. Only 10 (22%) mothers with affected pregnancies had a diagnosis of primary SS at the time of diagnosis of the first pregnancy complicated by CHB (a mean of 4 years before, ranging from 1 to 10 years). In 6 (14%) mothers, primary SS was diagnosed during pregnancy or less than 12 months after the delivery/termination. In the remaining 28 (64%) mothers, pSS was confirmed 1-5 years after CHB diagnosis (n=19, 68%), 6-10 years after (n=2, 7%), or more than 10 years after the first case of CHB was diagnosed (n=7, 25%). CHB was diagnosed in uterus

in all cases but two. AV block was initially incomplete in 11 fetuses and complete in 36 (no available data in 2 cases). Among the 35 (71%) surviving children with CHB, 5 (14%) developed other features of neonatal lupus. After the index pregnancy, 12 women had 20 subsequent pregnancies: five were complicated by a CHB (recurrence rate of CHB of 25%). The 4 women who had recurrent CHB were double-positive for anti-Ro and anti-La antibodies, and all had a confirmed pSS before having the first index case of CHB.

Conclusion. In pSS, autoimmune CHB could be one of the first "indirect" signs of the disease in women of child-bearing-age, in whom the diagnosis is confirmed several years later. Some maternal characteristics could be related with recurrent CHB, such as having an already-confirmed diagnosis of pSS and carrying the two Ro/La autoantibodies.

Introduction

Autoimmune congenital heart block (CHB) is an immuno-mediated acquired disease related to the placental transference of maternal anti-Ro/La antibodies that is included under the umbrella of different manifestations collectively referred to as neonatal lupus (1). These features are associated with the placental transference of maternal antibodies against Ro/La autoantigens, and has been related not only to the development of cardiac abnormalities, but also to cutaneous rash, liver damage and cytopenias in the newborn (2). With respect to autoimmune CHB, anti-Ro/La antibodies begin to cross the placenta as early as 11 weeks of gestation, and the autoimmune damage of fetal conduction tissues leads

to blockage of signal conduction at the atrioventricular (AV) node after causing inflammation and fibrosis (3). The great majority of affected babies present with third-degree (complete) AV block (4), resulting in a severe reduction in the normal fetal ventricular heart rate, often ranging between 50 and 70 beats per minute (5). Autoimmune CHB is a very rare disease, with an estimated incidence of 1:20,000 live births (1).

In 1928, Aylward (6) reported the first case associated with a maternal autoimmune disease (Mikulicz's disease), while several studies in the 1960s and 1970s linked CHB to maternal systemic lupus erythematosus (SLE) (7-9). Since then, SLE has been overwhelmingly considered the key maternal systemic autoimmune disease to be investigated in mothers having babies with autoimmune CHB. In contrast, Sjögren's syndrome (SS) has been related to CHB mainly in isolated case reports (10-12), despite considering that the frequency of anti-Ro/La antibodies in primary SS (pSS) is 2/3-times higher than in SLE (13, 14), and that pSS is a systemic autoimmune disease more prevalent than SLE in the general population (15). During decades, systemic features of pSS have been heterogeneously defined and classified, making impossible to have a clear view about the frequency and clinical presentation of systemic SS (16). In 2010, a specific EULAR task force developed the EULAR-SS disease activity score (ESSDAI) (17), allowing a homogeneous evaluation of systemic disease and thus representing a step forward in the evaluation of complex SS. However, there is an increasing number of reports in patients with pSS identifying systemic features not included in the current ESSDAI classification, such as autoimmune CHB, studies that are suggesting that systemic SS may be wider than that covered by the ESSDAI classification (18).

The objective of the current study was to characterise the autoimmune CHB associated with a maternal diagnosis of pSS confirmed either before, concomitant or after the first pregnancy complicated with autoimmune CHB.

Methods

Patients

The Big Data Sjögren Project Consortium is an international, multicentre registry designed in 2014 to take a "high-definition" picture of the main features of pSS using worldwide data-sharing cooperative merging of pre-existing clinical SS databases from leading centres in clinical research in SS from the five continents (see reference 19 for additional methodological details) (19). The centres share a harmonised data infrastructure and conduct cooperative online efforts in order to refine already-collected data in each centre, under the coordination of two data scientists (NAD and BK). Inclusion criteria were fulfilment of the 2002 classification criteria (20). Exclusion criteria for considering SS as a primary disease were chronic HCV/HIV infection, previous lymphoproliferative processes, and associated systemic autoimmune diseases. Diagnostic tests for SS (ocular tests, oral tests and salivary gland biopsy) were carried out according to the recommendations of the European Community Study Group (21). The study was approved by the Ethics Committee of the Coordinating Centre (Hospital Clinic, Barcelona, Spain, registry HCB/2015/0869).

Definition of variables

The following inclusion criteria were applied: (i) Mothers with positive Ro/La autoantibodies detected previously or at the time of diagnosis of the first case of CHB; (ii) diagnosis of CHB confirmed by fetal echocardiography; (iii) AV block diagnosed *in utero*, at birth or within the neonatal period (0-27 days after birth) (8); (iv) absence of anatomical cardiac abnormalities which might be causal of AV block; and (v) maternal fulfilment of the 2002/2016 SS criteria before, during or after having a pregnancy complicated with CHB. Cases containing insufficient, unclear information on the characteristics of CHB were excluded, as well as mothers presenting concomitant systemic autoimmune diseases other than primary SS.

Information about the following fetal and maternal features was retrospec-

tively collected: maternal autoimmune diseases diagnosed before the first case of CHB (index case), maternal age at diagnosis of pSS (age at fulfilment of the 2002 criteria), positive immunological markers detected before/during pregnancy, previous systemic therapies related to underlying autoimmune diseases, maternal age when pregnancy was confirmed, active treatments at the time of becoming pregnant, treatments maintained once pregnancy is confirmed, week of pregnancy of first obstetric ultrasound, week of pregnancy confirming cardiac disease, diagnostic tests used for confirming cardiac disease, classification of CHB (grades I, II, III), other cardiac abnormalities (endocardial fibroelastosis, valvulopathy, other arrhythmias), specific therapy of congenital heart block (agent, dose, duration), pregnancy termination (voluntary termination of pregnancy, fetal death), week of pregnancy at termination, outcome of the cardiac block/damage (progression or regression of heart block, other cardiac damage), other extracardiac complications (serositis, hydrops), week of pregnancy at delivery, maternal age at delivery, delivery (natural, induced, caesarean section), heart block type at delivery, other clinical features present at delivery (cutaneous, liver, hematological), autoimmune diseases diagnosed after delivery (specify disease and maternal age), and outcome of the baby (pacemaker, transplantation, autoimmune diseases, death).

With respect to SS, disease diagnosis was defined as the time when the attending physician confirmed fulfilment of the 2002 criteria. The main disease features at this time were retrospectively collected and analysed. The following clinical variables were selected for harmonisation and further refinement: age, gender, ethnicity, country of residence, fulfilment of the 2002 criteria items, antinuclear antibodies, rheumatoid factor, C3 and C4 levels, cryoglobulins, and organ-by-organ ESSDAI scores. Systemic involvement at diagnosis was retrospectively classified and scored according to the ESSDAI (17), which evaluates 12 domains or organ systems.

Statistical analysis

Descriptive data are presented as mean and standard deviation (SD) for continuous variables and numbers and percentages (%) for categorical variables. The non-parametric test Fisher's exact test was used for testing independence in 2x2 contingency tables comparing dichotomic variables in mothers with and without recurrent CHB. All significance tests were two-tailed and values of $p < 0.05$ were considered significant. p -values were not adjusted for multiple testing because the hypothesised associations were specified *a priori*. All analyses were conducted using the R v. 3.5.0 for Windows statistical software package (<https://www.R-project.org/>).

Results

We identified 49 cases of autoimmune CHB in children born from 44 mothers who had a mean age at the time of pregnancy of 30.3 years (range 18 to 41). At the time of diagnosis of autoimmune CHB, all mothers had positive anti-Ro antibodies and 28/44 (64%) were positive for anti-La antibodies. Most mothers have no diagnosis of systemic autoimmune disease at the time of diagnosis of the first autoimmune CHB. Only 10 (22%) mothers with affected pregnancies had a diagnosis of pSS at the time of diagnosis of the first pregnancy complicated by CHB (a mean of 4 years before, ranging from 1 to 10 years). In 6 (14%) mothers, pSS was diagnosed during pregnancy or less than 12 months after the delivery/termination. In the remaining 28 (64%) mothers, there was no diagnosis of a defined systemic autoimmune disease but were followed as asymptomatic Ro/La carriers or as having an undifferentiated autoimmune disease. Among them, pSS was confirmed 1-5 years after CHB diagnosis ($n=19$, 68%), 6-10 years after ($n=2$, 7%), or more than 10 years after the first case of CHB was diagnosed ($n=7$, 25%). (Table I). Figure 1 summarises the outcomes of the 44 mothers. CHB was diagnosed *in utero* in all cases but two, that were diagnosed within the neonatal period. Detailed information about the week of pregnancy at the time of CHB diagnosis was available in 35 cases: AV block was diagnosed

Table I. Main features of mothers with pSS having a pregnancy with autoimmune CHB.

	Mothers with pSS (n=44)
Maternal age at the time of first CHB case, years (mean, range)	30.3 (18-41)
Maternal age at the time of SS criteria fulfillment, years (mean, range)	34.1 (19-60)
Immunological markers	
Anti-Ro antibodies	44 (100%)
Anti-La antibodies	28/44 (64%)
Immunological Ro+ status	
Positive before first CHB case	13 (30%)
Positive detected at the first pregnancy with CHB	31 (70%)
Fulfillment of SS criteria	
Before first CHB case	10 (22%)
Concomitant	6 (14%)
After first CHB case	28 (64%)
Diagnosis of pSS after first index CHB case	
1-5 years	19 (68%)
6-10 years	2 (7%)
>10 years	7 (25%)
CHB recurrent rate	
Mothers with subsequent pregnancies after the first CHB case	12
Number of pregnancies	21
Mothers who had subsequent pregnancies complicated with CHB	4
Number of pregnancies with CHB	5
Recurrence rate	5/21 (24%)

pSS: primary Sjögren's syndrome; CHB: congenital heart block.

before the week 20 in 6 cases (17%), between weeks 20-24 in 23 (66%), and after the week 25 in the remaining 5 (14%) cases. Information about the type of CHB and associated therapies was available in 47 cases. AV block was initially incomplete in 11 (23%) fetuses (5 first-degree and 6 second-degree CHB), and complete in 36 (77%, third-degree CHB). With respect to treatment, 7 mothers received hydroxychloroquine (in 6, the drug was started before the pregnancy and was maintained, while in the remaining case, the drug was introduced after the CHB diagnosis), 18 received fluorinated steroids (mainly dexamethasone in 16) in combination with intravenous immunoglobulins and plasma exchanges in 4 cases. We observed the following outcomes according to the CHB type. Among the 5 cases of first-degree AV block, 4 disappeared (three after maternal treatment with fluorinated steroids, in one case associated with intravenous immunoglobulin (IVIG) and plasma exchanges) and one persisted at the time of delivery; while among the 6 second-degree AV blocks, four progressed to complete AV block despite treatment, one remained un-

changed at the time of delivery and one reversed to type I block (both treated with fluorinated steroids). None of the fetuses diagnosed with complete AV block (including 11 cases treated with fluorinated steroids) regressed, and there were 12 elective terminations of pregnancy and two intra-uterine fetal deaths due to progressive severe cardiopathy (Table I).

Among the 35 (71%) surviving children with CHB (4 born preterm, 13 requiring cesarean delivery), 5 (14%) developed other features of neonatal lupus including raised liver enzymes ($n=3$), cutaneous subacute lupus ($n=2$) and thrombocytopenia ($n=1$); and 23 (66%) had a pacemaker implanted before the 6 months of life ($n=15$), between 6 months and 2 years-old ($n=5$) and after 2 years-old ($n=2$). Two children who received a pacemaker died (at 4 and 8 years-old, respectively), and other required a heart transplantation in the adulthood.

After the index pregnancy, 12 women had 20 subsequent pregnancies: five were complicated by a CHB, and therefore, the recurrence rate of CHB in our cohort was 25% (Table II). AV

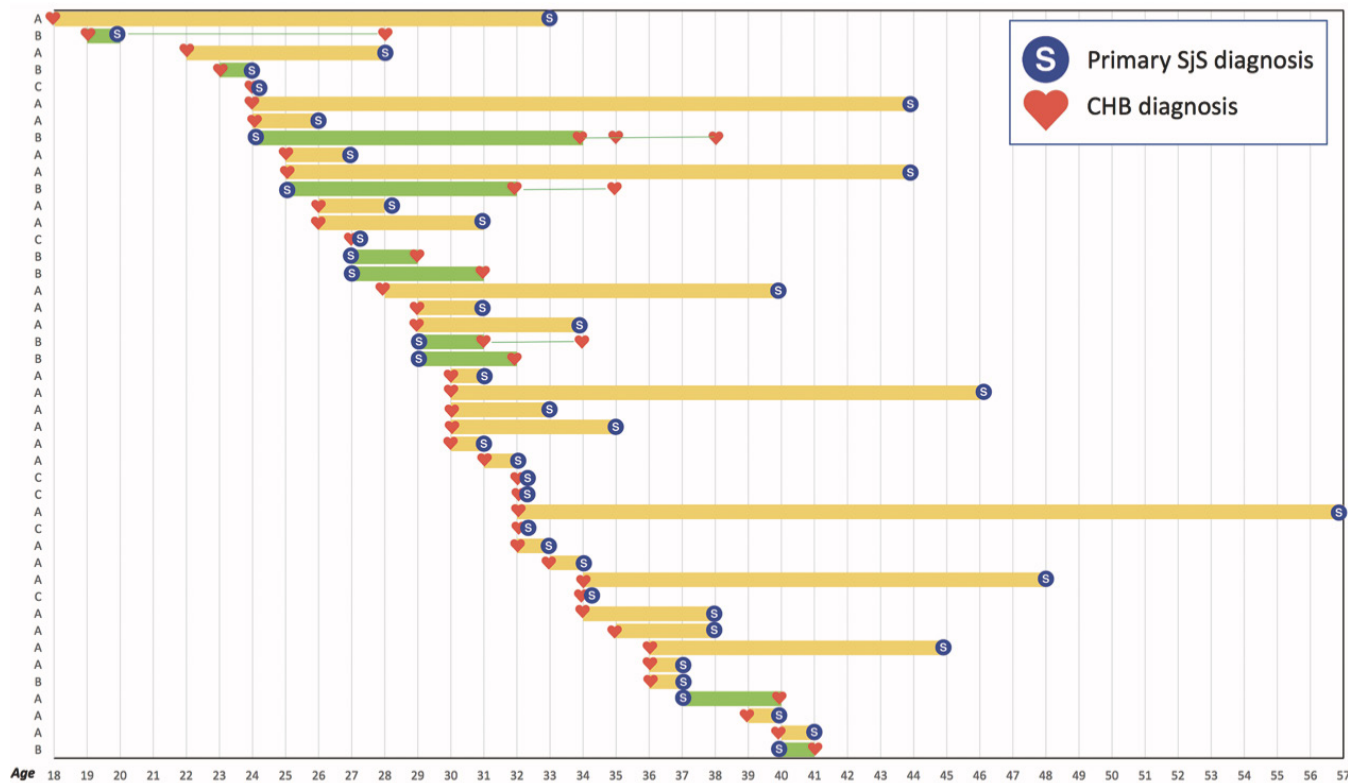


Fig. 1. Outcomes of 44 mothers with pSS and autoimmune CHB according to the maternal age. A: diagnosis of pSS confirmed after first case of CHB (yellow bars); B: diagnosis of pSS confirmed before first case of CHB (green bars); C: concomitant diagnosis of pSS and CHB (no bar). Recurrent CHB (green lines).

block was initially incomplete in 2 fetuses (1 first-degree and 1 second-degree CHB), and complete in 3 (third-degree CHB). Among the two cases of incomplete AV block, one disappeared (1st degree), while the second-degree AV block progressed to complete AV block despite receiving treatment with dexamethasone. There were 3 (60%) elective terminations of pregnancy and two (40%) children born alive. Among the 2 surviving children with CHB, one had a pacemaker implanted before the 6 months of life. Interestingly, the 4 women who had recurrent CHB (3 had one recurrent CHB, one had two cases of recurrent CHB) shared two features: all were double-positive for anti-Ro and anti-La antibodies, and all had a confirmed pSS before having the first index case of CHB. Therefore, the rate of recurrence in these mothers was of 100% (5 recurrences in 5 pregnancies), while no recurrence was reported in the 15 subsequent pregnancies from mothers who were asymptomatic carriers at the time of CHB diagnosis (100% vs. 0%, $p<0.001$). With respect to au-

toantibodies, the frequency of double positivity (Ro/La) in mothers with recurrent CHB was 100% in comparison with that in mothers without recurrence that was 50% ($p=0.077$).

Discussion

Ro/La autoantibodies, the key immunological markers of SS, are central in the aetiopathogenesis of the autoimmune CHB development (22). The body of evidence is based not only on a large number of epidemiological and clinical studies, but also on various *in vitro* and *in vivo* experimental studies (23, 24). AV block is the cardiac manifestation diagnosed in the affected fetus of mothers carrying Ro/La autoantibodies. Two specific characteristics of autoimmune CHB should be highlighted: AV block is predominantly diagnosed during a very-specific window of time (16–30 weeks of pregnancy), and the babies are overwhelmingly affected by the more severe form of block (complete block) (1). In consequence, autoimmune CHB is associated with a significant mortality rate (nearly 20%),

and the majority of deaths (70%) occur *in utero* mainly due to severe cardiomyopathy (1). Despite the very rare frequency of autoimmune CHB, the high rate of fetal mortality and the very high frequency of pacemaker requirement in the survivors makes the condition as a life-threatening obstetrical complication (25, 26).

To the best of our knowledge, this is the first study totally focused on the development of autoimmune CHB in mothers with pSS, and our data reinforce the importance of SS as a cause of CHB since this condition is frequently underdiagnosed at the time of pregnancy/birth. We found that only around 20% of mothers had a confirmed pSS at the time of their first pregnancy complicated by CHB. In fact, the majority of mothers with affected pregnancies lacked a diagnosis for a specific autoimmune disease. Analysis of underlying diseases in nearly 900 affected mothers showed that more than half were classified as asymptomatic carriers of anti-Ro/La antibodies, 15% had SLE, 14% pSS, 14% were classified as having an

Table II. Main features of pregnancies affected by autoimmune CHB from mothers with primary SS.

	Pregnancies with CHB (n=49)
Diagnosis of CHB	
In utero	47 (96%)
Neonatal (< 1 month)	2 (4%)
Weeks of pregnancy at in utero diagnosis of AV block (weeks)	
16-17w	1/35 (3%)
18-19w	5/35 (14%)
20-24w	23/35 (66%)
25-29w	4/35 (11%)
30-34w	1/35 (3%)
35-40w	1/35 (3%)
Cardiac block type	
III	36/47 (77%)
II	6/47 (13%)
I	5/47 (10%)
Other cardiac complications	
EFE	1/47 (2%)
Pericardial effusion	1/47 (2%)
Valvular disease	3/47 (6%)
Treatment	
Nothing	29/47 (62%)
Fluorinated corticosteroids	18/47 (38%)
Hydroxychloroquine*	7/47 (15%)
Intravenous immunoglobulins	4/47 (9%)
Plasma exchanges	4/47 (9%)
Pregnancy outcomes	
In uterine mortality	14/49 (29%)
Prematurity (<37 weeks)	4 (11%)
At term	18 (51%)
Caesarean	13 (37%)
Neonatal lupus features	
Cutaneous lupus	2/35 (6%)
Raised liver enzymes	3/35 (9%)
Thrombocytopenia	1/35 (3%)
Follow-up of babies	
Pacemaker	23/35 (66%)
Time of pacemaker	
<6 months	15/22 (68%)
6 months - 2 years	5/22 (23%)
>2 years	2/22 (9%)
Heart transplant	1/35 (3%)
Death	2/35 (6%)

*HCQ maintained (n=6) or introduced after diagnosing CHB (n=1).

CHB: congenital heart block; EFE: endocardial fibroelastosis; AV: auricular-ventricular.

incomplete or undifferentiated autoimmune disease, and less than 2% were diagnosed with other autoimmune diseases (1). The reason why the majority of affected mothers are asymptomatic could be related to the fact that anti-Ro and anti-La antibodies may appear several years before the clinical diagnosis of SLE or pSS (27, 28).

In our study, 64% of mothers were diagnosed with pSS at least one year after having the first pregnancy with CHB (a mean time of 7.36 years after). Previous studies evaluated the development of a full systemic autoimmune disease in asymptomatic mothers at the time of CHB development, and found that among 242 mothers who were followed a mean of 5 years (ranging from 1 to 11 years), the disease more frequently confirmed was SS (18%) followed by SLE (9%) (29-33). All our patients had positive Ro autoantibodies at the time of the first pregnancy complicated by CHB, and 65% had concomitant anti-La antibodies, a higher frequency than that reported in unselected series of CHB (4). The potential effect of carrying the two autoantibodies (anti-Ro and anti-La) has been evaluated in some earlier studies that suggested that the higher the number of maternal autoantibodies against the three antigens (Ro60, Ro52, La), the highest the risk of developing CHB, and a lower incidence of CHB in mothers carrying isolated anti-Ro antibodies has been reported in comparison with those carrying Ro and La autoantibodies (4). In contrast, the presence of maternal anti-La antibodies in the absence of anti-Ro antibodies is testimonial, representing <1% of all reported cases (4), and none of our affected mothers had isolated La autoantibodies. With respect to the type of CHB, we found that 77% of cases were classified as complete type III AV block, a similar figure than that reported for unselected cases of autoimmune CHB (1). With respect to the time of CHB diagnosis, we found 2 cases diagnosed before the 18 weeks of gestation (two cases diagnosed at 16 and 17 weeks, respectively), an early CHB diagnosis that has also been reported previously (1). In the largest review of autoimmune CHB cases, AV block was diagnosed between weeks 20-24 in more than half the cases, and in 75% between the weeks 20 and 29, with only 2% being diagnosed at birth or within the neonatal period (1). The distribution of the time of CHB diagnosis we found in our study was very similar (66% of our cases were diagnosed between weeks 20-24).

The rate of in utero mortality in our series was 29%, higher than that reported in a large review focused on unselected cases of autoimmune CHB (19%) (1), and we found that 70% of babies with autoimmune CHB required pacemaker, a very close figure than that reported for unselected cases (4). The variability in the clinical presentation of CHB in live births is a challenge for pediatric cardiologists, especially with respect to whom to pace and when (2). Two-thirds of babies are paced overwhelmingly during the first year of life and, in nearly two thirds of cases, during the first 10 days after birth (4). In addition, we found that 14% of babies presented with neonatal lupus, a similar figure than that previously reported in mothers carrying Ro autoantibodies (34). Babies born with autoimmune CHB require a close follow-up, since a quarter of total deaths related to autoimmune congenital heart block (ACHB) are reported during the first year of life, although in our series, the two deaths were reported later.

Due to the severity of ACHB, it is essential to know the risk of its development in women of childbearing age carrying Ro/La antibodies. This risk should be calculated from studies prospectively designed to evaluate pregnancy outcomes in these mothers (1.7%) (1). However, the risk increases 8-times (16%) when these mothers have a subsequent pregnancy (1). In our study, we found a higher recurrence rate (24%) and some specific maternal characteristics that could explain this higher figure. First, we found that all the mothers who experienced a recurrent CHB had a pSS diagnosed several years before having the first pregnancy complicated by CHB. A pooled analysis of prospective studies that detailed maternal disease in both affected and non-affected pregnancies showed that the recurrence rate of CHB was two-fold higher in mothers with SS and/or SLE (23%) compared with those with undifferentiated diseases or without disease (812%) (1), suggesting that mothers already-diagnosed with pSS at the time of CHB could be at high risk of developing recurrence in subsequent pregnancies. In addition, the mothers who experienced recur-

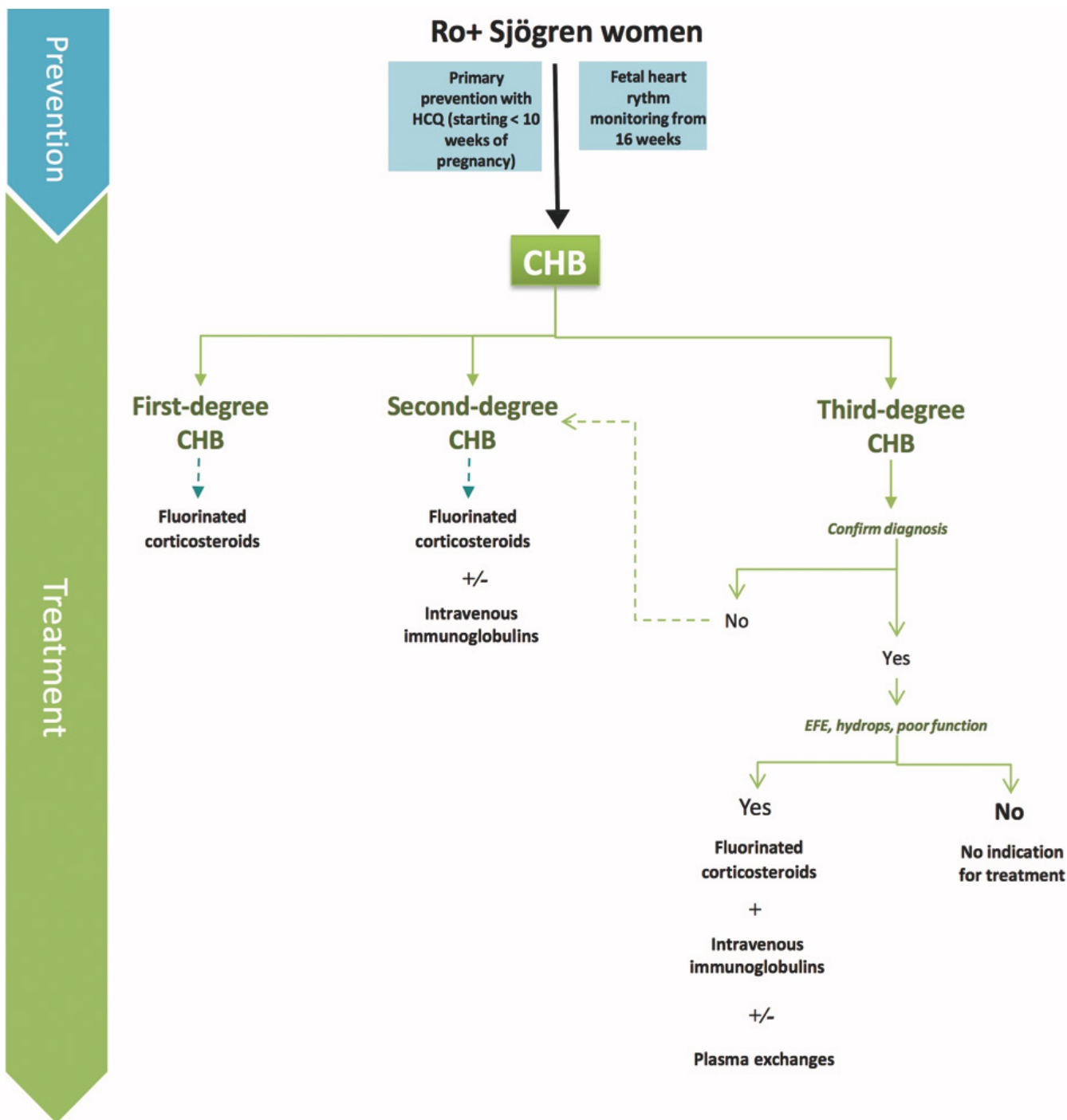


Fig. 2. Therapeutic recommendations for management of autoimmune CHB in mothers with SS carrying Ro autoantibodies. (Authors: Buyon JP, Izmirly PM, Khamashta M, Ramos-Casals M, Brito-Zerón P: CHB subgroup study of the EULAR SS Task Force) (40).

rent CHB in our study were all double-positive Ro and La autoantibodies, and a previous study using a multivariate analysis found a statistically significant trend for poor pregnancy outcomes in mothers with an established diagnosis of SS/SLE or carrying concomitant anti-La antibodies (1). Pregnant Ro/La+ carriers should be considered as women with a potential

high-risk pregnancy, and should therefore be followed by a highly specialised obstetric unit. Women who have babies with CHB of any degree, endocardial fibroelastosis (EFE), or congenital valvular disease should be tested for the complete Ro/La panel (1). Serial echocardiograms and obstetric sonograms should be performed weekly from 16 weeks of gestation onwards, although the fre-

quency might be reduced in the absence of CHB after the 26th week, since less than 20% of cases are diagnosed after the 30th week of gestation (1). Newborns might reasonably be followed during the first month of life, since 2% of reported cases of CHB are diagnosed postnatally (<27 days after birth). Physicians caring for women of childbearing age carrying anti-Ro/La antibodies

must offer solid, updated information when mothers ask about the risk of having a baby with autoimmune CHB (35). Another key aspect is the therapeutic approach of this severe complication. Until now, no effective treatment has been reported for reversion of complete AV block (36), while for incomplete AV block, the use of fluorinated corticosteroids, IVIG and plasma exchanges has been suggested (3). Probably, the key therapeutic approach must be prevention more than treatment of an established AV block. Ruffatti *et al.* (37) concluded that a combined therapy consisted of weekly plasmapheresis, fortnightly intravenous immunoglobulins (IVIG), and daily 4 mg betamethasone from CHB detection until delivery seems to be effective and safe in treating second degree CHB. The safety of hydroxychloroquine use during pregnancy was first reported in case studies (38). Recently, a multicentre, open-label, single-arm, clinical trial including mothers with a previous pregnancy complicated by CHB used 400 mg daily of hydroxychloroquine (HCQ) (prior to completion of gestational week 10, and then maintained through pregnancy), and have reported that HCQ significantly reduces the recurrence of CHB below the historical rate by >50% (39). In this regard, we recommend to follow the EULAR recommendations for SS about the therapeutic management of autoimmune CHB (40) (Fig. 2).

The study has some limitations. With a retrospective design analysing pre-existing data obtained from medical records, a recall bias cannot be discarded. In addition, the physician assessment and the referral patterns from each centre may influence how the cases were detected and captured. Furthermore, and also related to the retrospective data collection, there was no information about other autoantibodies that have been related with autoimmune CHB (anti-Ro52, anti-Ro60, anti-p200 antibodies); other immunological details such as the titres of anti-Ro antibodies or the use of native vs. recombinant antigens in the immunological techniques, have not been evaluated.

Autoimmune CHB is undeniably a severe, potentially life-threatening disorder

associated with the passive transfer of maternal Ro/La autoantibodies. Although until now most studies have supported a predominant role of SLE as the maternal disease that should be always investigated after diagnosing a baby with CHB, we support that ACHB may be mainly related to SS, either undiagnosed or preclinical, and either primary or in association with SLE. The severity of ACHB is perfectly illustrated by a global mortality rate of 20% and a rate of 64% of pacing of live births. We found that some maternal characteristics could be related with recurrent CHB, such as having an already-confirmed diagnosis of pSS and carrying the two Ro/La autoantibodies. In pSS, ACHB could be one of the first “indirect” signs of the disease in women of childbearing-age, in whom the diagnosis is confirmed several years later.

Affiliations

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