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Atrial fibrillation in pregnant women – guidelines for treatment. Own experience based on four clinical cases

Migotanie przedsionków u kobiet w ciąży – zasady postępowania i leczenia. Doświadczenia własne na podstawie opisu czterech przypadków

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Słowa kluczowe

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Summary

Cardiac arrhythmia in pregnant women, including atrial fibrillation, is an important clinical problem. Doctor taking diagnostic and therapeutic actions is responsible for the health of both mother and child. Most cases of the cardiac arrhythmia are mild and occur in the 3rd trimester, 50% of cases are asymptomatic, every second pregnant woman has premature ventricular and supraventricular contractions. Atrial fibrillation concerns about 1% of all cardiac arrhythmias diagnosed during pregnancy, it is rare arrhythmia for pregnant women who do not suffer from structural heart condition and prior history of the atrial fibrillation. The procedure depends on the etiology, which is diverse for pregnant women. In 52% of all cases arrhythmia episodes concerns women with prior diagnosed abnormal heart rhythms. For this cases higher percentage of fetal complications is diagnosed. Bearing in mind the wellbeing of both mother and child, proper and quick diagnosis are crucial along with appropriate choice of medication. Both pharmacological and electrical cardioversion are allowed during pregnancy. However it is important to remember that the target therapeutic procedure at the end of the pregnancy is electrophysiology study and arrhythmia ablation.

In this paper we present four cases of pregnant women with atrial fibrillation with different clinical course, treatment, etiology and complications.

Streszczenie

Zaburzenia rytmu serca u kobiet w ciąży, a wśród nich migotanie przedsionków, to istotny problem kliniczny. Podejmując działania diagnostyczne i terapeutyczne, lekarz odpowiada zarówno za zdrowie matki, jak i dziecka. Większość zaburzeń rytmu serca ma charakter łagodny, najczęściej występuje w III trymestrze ciąży, 50% przebiega bezobjawowo, a u co drugiej ciężarnej występują przedwczesne skurcze komorowe i nadkomorowe. Migotanie przedsionków dotyczy ok. 1% wszystkich zaburzeń rytmu serca stwierdzanych w ciąży, jest rzadką arytmią u kobiet w ciąży bez strukturalnej choroby serca i wcześniejszego wywiadu migotania przedsionków. Postępowanie jest zależne od etiologii, która u kobiet ciężarnych jest zróżnicowana. W 52% przypadków napady arytmii w ciąży dotyczą kobiet z wcześniej rozpoznanymi zaburzeniami rytmu. W tych przypadkach stwierdza się większy odsetek powikłań płodowych. Mając na uwadze zarówno dobro matki, jak i dziecka, bardzo istotne jest właściwe i szybkie postawienie właściwego rozpoznania oraz odpowiedni dobór leków. Zarówno kardiowersja farmakologiczna, jak i elektryczna mogą być stosowane w ciąży. Należy jednak pamiętać, iż docelowym postępowaniem terapeutycznym, po zakończeniu ciąży, może być badanie elektrofizjologiczne oraz ablacja podłoża arytmii.

W pracy przedstawiliśmy cztery przypadki kobiet ciężarnych, u których wystąpiło migotanie przedsionków, różniące się przebiegiem klinicznym, sposobem leczenia, etiologią i powikłaniami.

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CASE 1 (W.M.)

The patient, 28 years old, 7th week of 4th pregnancy, with poor obstetric history (two miscarriages in early pregnancy), after surgical correction of the heart defect in 1992 (ventricular septal defect ASD type II, patent ductus arteriosus, supravalvular pulmonary stenosis) with implanted heart chamber pacing system due to the sick sinus syndrome and paroxysmal atrial flutter (in 1992).

Additionally prior history of the extraction of the ventricular pacing lead and implantation of the cardiac pacing (in 2011). Echocardiography showed tricuspid insufficiency 2nd/3rd degree. Furthermore prior history of paroxysmal atrial flutter and hepatitis C. The patient was admitted to Outpatient Cardiology Clinic for Pregnant Women in Lublin, treated with Sotalol 40 mg 1 x 1 tablet and Acetylsalicylic Acid 75 mg 1 x 1 tablet. The electrocardiogram examination showed atrial fibrillation with irregular ventricular function ca 70/min and right bundle branch block, duration of atrial fibrillation was difficult to determine. The patient did not feel the arrhythmia. The patient was referred to Cardiology Department in order to stabilize atrial fibrillation. On admission the patient's condition was stable, with proper circulatory and respiratory parameters, pregnancy alive. Physical examination: visible scar after correction of the heart defect, irregular heart rate 70-100/min, systolic murmur (Levine 3/6) above pulmonary artery, RR 120/70 mmHg, no edema of lower limbs, above lungs normal vesicular murmur. Laboratory test with no significant irregularities, β-HCG – 36048.0 mIU/ml (indicating 8th week of the pregnancy). During observation in the cardiac intensive care unit the patient reported spotting/bleeding from the genital tract, she had multiple gynecological consultations. Fetal ultrasound was performed couple of times, indicating alive pregnancy with the presence of intrauterine hematoma and normal progress of β-HCG. Due to the good tolerability of the arrhythmia, the decision on the restoration of the sinus rhythm was postponed till the stabilization of the obstetric condition. Due to spotting/bleeding from the genital tract the patient was moved to the Pregnancy Pathology Department. On the day of discharge she was receiving Enoxaparin 60 mg 1 x 1 s.c., Progesterone 2 x 100 mg vaginally, Drotaverine 40 mg 3 x 1 tablet, Dydrogesterone 10 mg 2 x 1 tablet. The patient's condition was gradually improving. In the laboratory tests the elevated level of antibodies against HCV (> 11) was found. The patient was discharged with the alive pregnancy with β-HCG levels corresponding with the age of pregnancy, with no spotting/bleeding, with proper circulatory and respiratory parameters with persistent atrial fibrillation. The patient was again hospitalized in 13th week of pregnancy due to the vaginal bleeding and abdominal pain lasting for several days. On admission the heart rate was irregular due to the atrial fibrillation, RR 130/80 mmHg, with proper circulatory and respiratory parameters. The ultrasound showed retained fetal heart rate. The laboratory tests showed slightly decreased blood cell count (RBC – 3.36, HGB – 11.0, HCT – 31%, MCV – 92.2), elevated level of GGTP 182.00 U/L (N < 31.00 U/L), with normal value of ALP 62 U/L, AST 18 U/L, total bilirubin 0.60 mg/dl, viral load of HCV was determined quantitatively (PCR method) at 3.79 x 10 to 5 IU/ml. The ultrasound showed widened pyelocalyceal system in the right kidney (1.57 cm) and initial section of the ureter (1 cm) with no visible changes in the liver. The patient condition was consulted with the gastroenterologist and infectious diseases specialist. The monitoring of the liver parameters every 2-3 weeks was recommended. The decision on the restoration of the sinus rhythm was postponed till the stabilization of the general condition of the patient. Throughout the hospitalization period the patient was apathetic and depressive, she was discharged at her own request before the end of therapeutic process. On the day of discharge she was receiving Enoxaparin 60 mg 1 x 1 s.c., Progesterone 2 x 2 tablet, Dydrogesteron 2 x 1 tablet, Metoprolol 2 x 25 mg. In the 25th week of the pregnancy the patient was admitted to the Gynecological and Obstetrics Emergency due to weak feeling of the fetal movements. On admission her condition was stable, with persistent atrial fibrillation with normal heart rate around 80/min (the patient did not feel the arrhythmia), RR 110/71 mmHg, normal vesicular murmur. The fetal ultrasound showed large lacunar fluid concentration with sedimenting content, on the fetal surface of the placenta, of total volume of over 250 ml, no signs of intrauterine growth restriction or anemia was determined in fetus. Prophylaxis of neonatal respiratory distress syndrome with betamethasonum was introduced. Obstetrical pessary was inserted. The electrocardiogram showed persistent atrial fibrillation, the patient did not feel the arrhythmia. On the day of discharge she was receiving Enoxaparin 60 mg 1 x 1 s.c., Metoprolol 50 mg 2 x 1/2 tablet, Progesterone vaginally 2 x 100 mg, Dydrogesteron 2 x 1 tablet. Due to the vaginal spotting/bleeding the enoxaparin dose was not altered. The patient gave preterm birth to a healthy boy (1600 g) in the 32nd week of the pregnancy via C-section due to premature abruption of the placenta. During checkup appointment in Cardiac Clinic the ECG showed regular sinus rhythm (spontaneous reversion to sinus rhythm). Currently patient is receiving Warfarin under INR control.

Conclusions

The presented case refers to a patient after correction of structural heart disease with atrial fibrillation of unknown duration. The decision on the restoration of the sinus rhythm was postponed till the end of pregnancy, with prior anticoagulant preparation and TEE examination. The patient was receiving 1 x 60 mg of enoxaparin subcutaneously. After the patient gave birth, there was a spontaneous recovery of sinus rhythm, the patient is receiving warfarin (INR control). The patient remains under constant monitoring of the Cardiology Clinic.

CASE 2 (S.A.)

The patient, 28 years old, 16th week of 1st pregnancy, with paroxysmal atrial fibrillation and history of paroxysmal supraventricular tachycardia with prolapse of the anterior leaflet of the mitral valve and 2nd degree regurgitation. The patient was admitted to Outpatient Cardiology Clinic for Pregnant Women. The electrocardiogram showed perpetual arrhythmia with atrial fibrillation, ventricular rate 80-100/min. The patient was not taking any medications. The patient presented the electrocardiogram results from April (same year) showing unstable cardiac rhythm – numerous extrasystole with single impulse with visible P-wave. The patient was unable to

determine when the arrhythmia started. The patient was referred to Cardiology Department order to stabilize heart rate. History of frequent recurring fainting with dizziness but no consciousness loss. On admission the patient's condition was stable, with proper circulatory and respiratory parameters, RR 95/55 mmHg, HR 100/min, normal vesicular murmur, pregnancy alive. Transesophageal echocardiography showed no thrombus, progression of mitral regurgitation (2nd/3rd degree) and tricuspid regurgitation (2nd degree), patent foramen ovale with slight left-to-right shunt. The electrical cardioversion gave no effect. Due to the stable condition of both mother and child, the attempt to restore sinus rhythm was postponed till the end of pregnancy. The patient was discharged from the hospital. Due to difficulties in contacting the patient and lack of cooperation oral anticoagulant therapy was abandoned and Enoxaparin 1 x 60 mg s.c. was recommended. Up to 34th week of pregnancy electrocardiogram showed atrial fibrillation. After giving birth the patient did not report to the Cardiology Clinic.

Conclusions

Patient with atrial fibrillation of unknown duration, patient did not feel the arrhythmia, she was not cooperative and did not comply with doctors recommendations. The electrical cardioversion attempt failed, sinus rhythm was not restored. After giving birth the patient did not continue treatment in the Cardiology Clinic.

CASE 3 (K.J.)

The patient, 37 years old 18th/19th week of 6th pregnancy, combine mitral regurgitation and stenosis, admitted to Neurology Department due to sudden paresis of the right lower limb and paralysis of right upper limb with mixed aphasia. The CT scan of head showed ischemic vascular area in the area of vascularization of middle cerebral artery. The echocardiogram showed no embolic material. It was determined that the paroxysmal atrial fibrillation due to mitral regurgitation and stenosis was the cause of the thromboembolic stroke. In the 33rd week of preganacy C-section was performed (during general anesthesia for C-section the temporary lack of aphasia was observed). Due to the mitral disease, after the C-section, the mitral commissurotomy and valvuolpastic was performed. The patient was receiving Acenocumarol (INR control), Digoxin 100 μg 1 x 1 tablet, Potassium 2 x 1 tablet. She continued her treatment in the Cardiology Clinic. The ECG showed sinus rhythm. Physical examination: regular heart rate 80/min, right-hand hemiparesis, motor aphasia. The patient was receiving (for a long period of time but very irregularly) Acenocumarol (INR control), Digoxin 100 mg 1 x 1 tablet, Nitrendipine 2 x 10 mg. During checkup appointment, the patient was diagnosed with atrial fibrillation. She was referred to the Cardiology Department in order to stabilize heart rhythm. The transesophageal echocardiography ruled out thrombus in the left atrial appendage and showed mitral valve restenosis with insufficiency 2nd/3rd degree, with the area of the left vein orifice 1.2-1.3 cm^2, maximum gradient 19.7 mmHg, medium 7.4 mmHg. Successful electric cardioversion (100 J) was performed. During cardioversion temporary asystole was observed. The patient was discharged from the Department in a fairly good condition, she was pre-qualified for percutaneous mitral valvuloplasty. During the next hospitalization coronary angiography was performed which ruled out significant changes in the coronary arteries, after surgical consultation patient was qualified for surgical treatment of the defect. In the Cardiac Surgery Department prosthetic mitral valve (ATS 27) was implanted along with RF ablation of the left atrium and left atrial appendage closure. Right after the procedure nodal rhythm was observed, the patient required temporary epicardial stimulation. In the following hours atrial fibrillation/atrial flutter were observed with the heart rhythm 75-130/min. On the 4th day of hospitalization electrical cardioversion was performed, temporary asystole was observed shortly after. The patient required epicardial stimulation. The electrocardiogram (with the use of Holter monitor) registered 1458 pauses > 2 s (including the longest one of 5375 ms) – the patient treated with metoprolol 12.5 mg 1 x 1 tablet. After discontinuation of treatment with beta-blocker – 69 pauses > 2 s over one day period (including the longest one of 3485 ms). The patient was diagnosed with tachy-brady syndrome and thus recommended treatment with constant electrostimulation. The atrial peacemaker was implanted. The procedure and further hospitalization was without complications. On the day of discharge from the hospital the patient was receiving Furosemide 1 + 1 + 0, Potassium 1 x 1 tablet, Spironolactone 25 mg 1 x 1 tablet, Metoprolol 25 mg 1 x 1 tablet in the morning, Sodium Valproate with Valproic Acid 300 1 x 1 tablet, Proton Pump Inhibitor 20 mg 1 x 1, Warfarin (INR controle). The patient is still monitored by the Cardiology Clinic, she requires third person assistance, contact with the patient is very difficult as she speaks only single words.

Conclusions

In this case study we described serious, long-term implications of the atrial fibrillation – brain stroke with lasting motor aphasia, paresis of the right lower limb and paralysis of right upper limb – the first symptom of the atrial fibrillation. Temporary lack of aphasia during general anesthesia for C-section gave some hope. The patient thanks to long-term rehabilitation and her husband's help is able to move on her own and speak a few words. She has been a patient of the Cardiology Clinic for 30 years now.

CASE 4 (T.E.)

The patient 33rd week of pregnancy, with the history of persistently recurring atrial tachyarrhythmias (atrial tachycardia with variable conduction block, atrial fibrillation). The first supraventricular arrhythmia incident happened in the 32nd week of pregnancy, the patient was not suffering from arrhythmia prior to pregnancy. During multiple hospitalization in the Cardiac Intensive Care Departemnt the sinus rhythm was restored both via pharmacological

cardioversion and electrical one (effective electrical cardioversion with the energy dose of 80J in 32 hbd, in 35 hdb ineffective electrical cardioversion with 100J, 125J and then 150J – the sinus rhythm was restored with pharmacological intervention). The patient was receiving Metoprolol 50 mg 2 x 1/2 tablet, Propafenone 150 mg 2 x 1 tablet, Digoxin 0.25 μg 1 x 1 tablet, Magnesium and Potassium salts 2 x 1 tablet and Enoxaparin 40 mg 2 times a day s.c. The C-section was performed due to obstetric indications, healthy boy was born (3390 g, 53 cm, 10 points – Apgar score). The patient was monitored by the Cardiology Clinic. After giving birth the patient underwent two RF ablation of the arrhythmia cause procedures. First ablation was performed in January 2011 – the right atrium (VCS), ineffective. Second procedure was performed in the Cardiology Institute in Anin, in February 2012 – left atrium, effective. At present the patient is in the 18th week of 2nd pregnancy, she is receiving ASA 75 mg 1 x 1 tablet. The echocardiogram shows sinus rhythm.

Conclusions

This case shows that both pharmacological cardioversion and electrical one can be safely performed during pregnancy. However ablation of arrhythmia cause may be the target therapeutic procedure, as in this case it proved to be effective method of treatment.

DISCUSSION

The atrial fibrillation cases in pregnant women with no organic heart disease or non-cardiac factors such as: hyperthyroidism, diabetes, systemic diseases, medications or electrolyte imbalance represent about 1% of all arrhythmia cases diagnosed during pregnancy. Changes that are affecting cardivascular system of a pregnant woman increases the possibility of arrhythmia (1). These include: increase of cardiac output by about 30-50%, increase in heart rate of about 10-20 beats per minute, increase of blood volume by 30-50%, decrease in vascular resistance, decreased hematocrit values, increased activity of renin-angiotensin-aldosterone system, decreased ANP level, increase of plasma concentration of catecholamines, and increase in adrenergic sensitivity (2, 3). The probability of arrhythmia occurrence increases with the presence of organic heart disease including the surgically corrected one (2). Thanks to incredible advances in cardiac surgery women with congenial or acquired heart defects are able to reach reproductive age and are willing to have children, thus atrial fibrillation and atrial flutter is an important and more frequent clinical problem. In 30 years of operation of the Outpatient Cardiology Clinic for Pregnant Women in Lublin atrial fibrillation accounted for 0.5% of all diagnoses. The majority of patients, are patients with structural heart diseases, after correction of heart defects or previously diagnosed atrial fibrillation. Interestingly more than a half of patients do not feel arrhythmia episodes and tolerate the condition very well. In this paper we presented four cases of different pregnant patients with atrial fibrillation. The decision on the type of pharmacotherapy should be always taken individually based on the patient's condition, week of pregnancy, severity and duration of arrhythmia, and patient's cooperation with the doctor. The doctors conduct is usually a compromise between beneficial influence on mother's cardiovascular system and potential toxic effect on the child (4). The most risky is pharmacotherapy during organogenesis period, i.e. in the first trimester. One should try to achieve a therapeutic effect with the lowest doses of antiarrhythmia medication possible, monitoring the condition of fetus (5). It is very difficult because the pharmacokinetics of drugs changes during pregnancy.

In accordance with the European Cardiac Society effective and worth considering first-line intravenous drugs in order to stop episode of atrial fibrillation are Ibutilide or Flecainide. Unfortunately the availability of both drugs in Poland is very limited (ibutilide is not available and flecainide is available only through specified purpose import). As a second option one can consider intravenous administration of propafenone or wernalakant. Due to its high toxicity for fetus, amiodaron can only be administered when other drugs are ineffective and arrhythmia is threatening life of mother and/or fetus. It has been proven that its use during pregnancy can cause fetal hypothyroidism, goitre, and growth inhibition in 9-17% cases. It can also cause bradycardia in neonates and QT interval prolongation lasting up to 7 days after birth (6).

Drugs controlling ventricular rhythm

First-line drugs in the control of ventricular rhythm are beta-blockers, mainly small doses of Metoprolol up to 50 mg/day (2 x 25 mg). It is important to remember that beta-adrenolytic drugs affect placenta and their use is associated with many adverse effects, including intrauterine growth retardation, respiratory disorders, bradycardia, and hypoglycemia in the newborn especially if the treatment was stared in early pregnancy (for example in 12-24th week). In case of pregnancy with complications due to the hypertension, if the patient was treated with propranolol, no congenial defects were observed in the child but there were reported cases of growth retardation in fetus. Atenolol administration no later than in the 1st trimester of the pregnancy was associated with the growth retardation in fetus as well. Second-line drug is digoxin which can be administered in case of contraindications to administer beta-blockers or non-dihydropyridine calcium antagonists, as well as in case of the occurrence of fetal cardiac tachyarrhythmias. It should be remembered that digoxin crosses the placenta with no limitations and drug poisoning in mother can cause death of the fetus. Data on use of Verapamil and Diltiazem are limited but oral administration of this drugs in order to control ventricular rhythm is considered to be safe (7). In 1996 cases of women receiving Verapamil and Diltiazem in the first trimester were reported and it seems that both drugs do not give major complications for the fetus (8).

Electrical cardioversion

The indicaton to perform electrical cardioversion during pregnancy are: hemodynamically unstable episode of atrial fibrillation, leading to hypotonia, heart failure, placen-

tal ischemia or ischemia of the central nervous system (9). The electrical cardioversion is considered to be a safe method in all stages of the pregnancy. It is recommended to use standard doses of energy, the impulse reaching the fetus is insignificant.

Anticoagulation therapy

During pregnancy we observe increased activity of the prothrombotic factors, so it is a condition predisposing to thromboembolic episodes. The occurrence risk increases 6 times during pregnancy and 11 times during childbirth. The patients without organic hearth disease or risk factors ("idiopathic" atrial fibrillation) are at low risk of embolic episodes and do not require anticoagulation or antiplatelet therapy before or during pregnancy. However research on pregnant women are not available, therefore it is very difficult to determine the ideal model of application of the blood-clot preventing drugs. The risk of embolism in nonvalvular atrial fibrillation in women who are not pregnant is evaluated based on the $CHADS_2$ criteria (10) or CHA_2DS_2-VASC scale (11). On these scales the benefits of anticoagulation therapy has been proven in cases when the risk of cardiovascular episodes was ≥ 4 cases for 100 patient-years (corresponding to ≥ 2 point on the $CHADS_2$ scale and 2 points on the CHA_2DS_2-VASC scale). Therefore the antithrombotic prophylaxis is recommended for high-risk patients including pregnant patients. The choice of anticoagulation therapy depends on the stage of pregnancy. As a prophylaxis it is recommended to use low-molecular-weight heparin incjection and Vitamin K Antagonists. Due to the high toxicity for the fetus new oral anticoagulants are not recommended. The Vitamin K Antagonists are recommended for most cases starting with the second trimester till about a month before the birth. The low-molecular-weight heparin or unfractioned drugs are safe for the fetus because they do not cross the placenta. Subcutaneous injections of low-molecular-weight heparin in therapeutic doses adjusted to body weight are recommended during the first trimester and in the last month of pregnancy. Low-molecular-weight heparin doses should be adjusted to the increasing body weight of the pregnant patient and to the concentration of anti-Xa.

CONCLUSIONS

The etiology of atrial fibrillation in pregnant women is very diverse, it includes organic heart disease as well as non-cardiac factors. There are however cases when the causes of cardiac arrhythmia cannot be clearly determined. The diagnostic and therapeutic procedure depends on the etiology.

The important factor is adequate protection of the pregnant patient with the atrial fibrillation from possible thrombotic complications. While selecting the best anticoagulation drug it is important to take into account the well-being of both the patient and the fetus, the dose should be adjusted to the clinical situation at hand. Due to the lack of broader research on anticoagulant theraphy of pregnant women the decision to include such treatment in the theraphy can be based on the CHA_2DS_2-VASC scale.

The cardiac arrhythmias in pregnant women can be treated effectively and in a safe way. However, the use of antiarrhythmic drugs in the first trimester (organogenesis period) should be avoided if possible, also the smallest doses possible should be administered.

Both electrical cardioversion and pharmacological one can be safely used during pregnancy. The electrical cardioversion is an effective treatment of the supraventricular tachyarrhythmias, associated with a low risk to mother and child.

The target therapeutic post partum procedure can be electrophysiological examination and ablation of the causes of the arrhythmia.

The pregnant patients with cardiac arrhythmia are multidisciplinary problem, their treatment requires a lot of experience.

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