

Appendicitis in diabetic pregnancy – case report

Zapalenie wyrostka robaczkowego u ciężarnej chorującej na cukrzycę typu 1 – opis przypadku

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Abstract

We present a case report of a 22-year-old pregnant patient with type 1 diabetes mellitus diagnosed with an appendicitis at 21st week of gestation, who underwent laparotomy and appendectomy. In later pregnancy, she required treatment for recurrent urinary tract infections and nephrolithiasis. Despite having several risk factors for an unfavorable perinatal outcome, she had caesarean section performed at term and delivered a healthy, full-term newborn. In this patient, we also discuss clinical conundrum of pregnancy complicated with several conditions that may manifest with acute abdominal symptoms and perioperative care for a pregnant woman with type 1 diabetes..

Key words: **appendicitis / pregnancy / appendectomy in pregnancy /
/ pregnancy in diabetic / type 1 diabetes mellitus /**

Streszczenie

Prezentujemy opis przypadku 22-letniej pierwotki chorującej na cukrzycę typu 1, z ropnym zapaleniem wyrostka robaczkowego w 21. tygodniu ciąży, wymagającym pilnego leczenia operacyjnego. Dalszy przebieg ciąży był powikłany nawracającymi infekcjami układu moczowego i kamicy nerkowej. Mimo licznych czynników ryzyka niekorzystnego wyniku położniczego (stan po przebyciu appendektomii, długotrwała cukrzyca, nawracająca kamica nerkowa), ciążę zakończono w terminie, cięciem cesarskim, porodem zdrowego, donoszonego noworodka. Na przykładzie omawianej sytuacji klinicznej przedstawiamy trudności diagnostyczne charakterystyczne dla ciąży powikłanej licznymi stanami mogącymi imitować objawy tzw. „ostrego brzucha” oraz specyfikę postępowania okołoperacyjnego w warunkach zagrożenia dekompensacją cukrzycy typu 1 u ciężarnej.

Słowa kluczowe: **zapalenie wyrostka robaczkowego / ciąża /
/ appendektomia w ciąży / cukrzyca przedciążowa /**

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Introduction

Appendicitis is one of the most frequent reasons of the so-called 'acute abdomen' during pregnancy with the incidence of 1:500-2000 pregnancies, most often in the second trimester [1, 2]. During pregnancy a false migration of the appendix from the right lower quadrant to the right upper quadrant of the abdomen takes place, as a consequence of passive displacement of the organ due to enlarging uterus. That is why symptoms from liver, pancreas, stomach and kidneys may hinder the diagnostic process of the disease [3, 4]. The pressure of the enlarging uterus on the appendix may mask the clinical symptoms and present an additional diagnostic difficulty.

The most reliable symptom remains to be pain in the right, lower quadrant of the abdomen. Tenderness, as well as abdominal guarding are not pathognomonic symptoms due to stretched abdominal muscles and the change in the position of the uterus between the appendix and anterior abdominal wall [1, 2, 5]. Weight loss, emesis and leukocytosis are frequent though non-specific symptoms and are typical for the first trimester of an uncomplicated pregnancy [6, 7].

On the example of the clinical situation presented in this article, the authors discuss diagnostic difficulties which a doctor may encounter when dealing with a pregnant woman suffering from type 1 diabetes mellitus with medical history, presenting with non-specific abdominal complaints. Such a situation calls for a multi-directional approach, taking into account pregnancy-related discomfort, complications of diabetes (gastroparesis or ketoacidosis) and conditions requiring surgical intervention. At the same time, while attempting to determine the reason for the complaints, maintaining normoglycemia should remain a priority.

Case report

A 22-year-old primipara at 21 weeks of gestation was referred to Obstetrics and Women's Diseases Clinic at Obstetrics and Gynecology Clinical Hospital of Poznań University of Medical Sciences due to acute abdominal complaints and nausea. The patient (weight 73kg, height 166cm) suffering from type 1 diabetes mellitus (White's class C, onset at age 12) was managed obstetrically since 10 weeks of gestation. Average daily glycemia was 99 mg/dl, HbA_{1c} was 7.8%, the patient was treated with Insulatard (26 units) and Actrapid (15 units) following a basal-bolus protocol.

Clinical examination upon admission revealed palpation tenderness in the right and middle (above the navel) abdominal region and slow bowel peristalsis. The patient reported renal colic before pregnancy, what additionally hindered the correct diagnosis. Blumberg's and Goldflam's signs were negative. Obstetric examination revealed normal nontender uterus, size corresponding to week of pregnancy. Vaginal fornix pain and adnexal tenderness were observed. Ultrasound examination revealed live fetus, no signs of premature placental abruption, normal adnexa. Surgical consultation was requested. Due to unclear symptoms and the necessity to exclude general illnesses which might mimic peritonitis, the surgeon recommended a 6-hour observation and additional diagnostic tests. Troponin levels were checked to exclude the possibility of coronary attack. Gasometry was performed to exclude ketoacidosis and general urine test was done to exclude renal colic or



Figure 1. Appendix in perioperative conditions.

bladder inflammation. Other laboratory tests revealed signs of inflammatory process: leukocytosis – 16.8 G/l (norm 4.10-10.90 G/l), granulocytosis – 13.7 G/l (norm 2.0-6.5 G/l). Elevated D-dimer levels were noted so differential diagnosis considered mesenteric arterial thrombosis. Average daily glycemia of the patient upon admission was 180mg/dl, HbA_{1c} was 5.9%. No emesis, normal stool. During observation Duphaston (2x1), Insulin Insulatard (6.30 – 16 IU, 22.00 – 10 IU.), Insulin Actrapid (8.00 – 5 IU, 12.00 – 5 IU, 18.00 – 5 IU), PWE (500ml), Dolargan (50mg), Fenoterol (1 amp. 0.5mg) and Isoptin (2 amp. 10mg/50 ml) were administered.

After 4 hours, due to increasing peritoneal symptoms, a reconnaissance laparotomy was performed and discovered purulent appendix (fig. 2), normal bowels and adnexa, corpus uteri corresponding to 22 weeks of gestation. Smear from the area of the appendix revealed the presence of *E. coli*.

The appendix was separated from its mesenteric attachment, purse-string suture was placed and securely tied, creating a residual appendiceal stump. After fixing the stump with sutures and controlling the bleeding, all abdominal layers were sutured and the skin was closed with continuous suture.

On day 1 after the surgery the patient was in good overall condition, non-febrile (36.6°C), average glycemia was 87 mg/dl, gasometry and electrolytes were within reference range. Physical examination revealed a soft, nontender, abdomen. Fetal movements were normal. For the next five days the patient was in good condition, did not complain, the wound healed well, average daily glycemia was 155mg/dl, HbA_{1c} 5.6%, fetal movements were normal. Antibiotic therapy, intravenous insulin therapy, hydration and tocolysis were continued. On day 7 after the operation the patient was discharged home in good overall condition, with recommendation to adjust current daily doses of insulin, keeping in mind hyperglycemic tendency resulting

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from inflammation, surgical treatment and necessary tocolytic therapy. At 30 weeks of gestation the patient was readmitted to the Clinic and diagnosed with urinary tract infection. Average glycemia was 85mg/dl, HbA_{1c} was 5.9%, insulin doses - Insulatard 26 IU, Actrapid 15 IU Furaginum (50mg) and Duphaston (10mg) treatment was initiated. After 4 weeks the patient was readmitted due to the threat of preterm labor and urinary tract infection (average glycemia was 90mg/dl, HbA_{1c} was 6.0%). Duphaston 10 mg, Hiconcil 500mg, No-Spa forte 80 mg, Papaverinum hydrochloricum WZF 40mg/2ml, Pyralginum 500mg/ml were administered.

At the end of 37 weeks of gestation the patient was yet again readmitted to the Clinic due to pain complaints that might suggest renal colic. Ultrasound examination revealed slight hydronephrosis and dilated ureter. At 38 weeks of gestation the pregnancy was ended with a cesarean section (indications: class C diabetes, appendectomy at 22 weeks of gestation, renal colic). The patient delivered a male baby, weight 3250g (Apgar 10, 10). After the delivery the overall condition of the patient was good, normoglycemia was achieved after correcting insulin doses postpartum (average glycemia on day 3 of the puerperium was 94mg/dl, HbA_{1c} was 6.3%, electrolytes and gasometry were normal). She was discharged home on day 4 after the cesarean section.

Discussion

Appendicitis is the most frequent non-gynecological cause of acute pain in pelvis minor in women and the most common indication for emergency surgery in pregnant women [8]. Incidence of acute appendicitis does not increase in pregnancy

but rupture of the appendix occurs 2-3 times more often due to delayed diagnosis and treatment, what influences perinatal mortality [8, 9]. The rate of misdiagnosis of appendicitis in reproductive-age women has been estimated to be 23.6-26.6%, and appendectomy is performed unnecessarily more often in women than in men (19% and 9% respectively), hence the importance of differential diagnosis [10, 11].

Acute cholecystitis is second most common cause of acute abdomen in pregnancy, with the incidence at 1:1600-10000 pregnancies [9]. In 90% of cases it is caused by cholelithiasis. Symptomatology in pregnant women does not differ from non-pregnant patients and the test of choice is an ultrasound examination due to its noninvasiveness and 95-98% sensitivity [12].

Intestinal obstruction is the third most frequent cause of acute abdomen in pregnancy, with the incidence at 1:1500- 16000 cases, especially in the third trimester [12, 13]. Postoperative adhesions occur in 60-70% of cases. Maternal and fetal mortality due to intestinal obstruction in pregnancy is significantly higher when compared to the rest of the population and rises with every trimester of pregnancy (up to 20% in the third trimester) [12]. The risk of intestinal volvulus is 25%, whereas in non-pregnant women the incidence is 3-5% [13, 14]. The probability of cecal volvulus may be 25-44% in patients with mechanical obstruction and is the highest at the time of rapid growth of the uterus in the third trimester of pregnancy [15, 16]. Nausea, persistent emesis, fever, leukocytosis and abnormal electrolyte concentrations ought to hint at obstruction but in pregnant patients with diabetes the cause may also be metabolic imbalance. The method of choice in such a case is the abdominal x-ray.

Table I. Recommended protocol of intravenous rapid-acting insulin infusion with syringe pump. Insulin concentration: 1 IU/1 ml 0.9% NaCl.

| glycemia | pump flow | insulin dose |
|---------------|--------------|--------------|
| <140 mg/mL | 1 ml/ hour | 1IU/ hour |
| 141-180 mg/mL | 1.5 ml/ hour | 1.5 IU/ hour |
| 181-220 mg/mL | 2 ml/ hour | 2 IU/ hour |
| > 220 mg/mL | 3 ml/ hour | 3 IU/ hour |

In case of no response to treatment – increase insulin flow speed

Table II. Recommended protocol of intravenous insulin infusion without the infusion pump.

| Glycemia | 5% glucose infusion | Number of rapid-acting insulin units added to every 500ml of 5%-glucose | number of drops per minute |
|---------------|---------------------|---|----------------------------|
| < 36 mg/mL | 500 ml | 0 | 84 |
| 36-70 mg/mL | 500 ml | 0 | 28 |
| 71-142 mg/mL | 500 ml | 6 | 28 |
| 143-214 mg/mL | 500 ml | 12 | 28 |
| 215-287 mg/mL | 500 ml | 16 | 28 |

In case of no response to treatment – increase insulin flow speed

Differential diagnosis in pregnant patients should also include more rare causes for acute abdomen such as thrombosis of the superior mesenteric artery or ovarian torsion. The latter is the cause of approximately 3% of emergency gynecological surgeries [17]. Pregnant women are at an increased risk of ovarian torsion: 25% of ovarian torsion cases are pregnant patients, most often in the first trimester of pregnancy and early puerperium [8]. In the event of ovarian torsion suspicion, the imaging test of choice is Doppler blood flow analysis.

Torsion of the ovarian stalk, commonly referred to as infundibulopelvic ligament, hinders the lymphatic, venous and eventually arterial flow what is detected by an ultrasound examination.

The incidence of appendicitis confirmed histopathologically after appendectomy is from 36% to 50% and decreases with every additional gestational week at the time of surgery [18, 19, 20]. Appendectomy has been proven to significantly more often cause premature labor than other non-obstetrical surgeries in pregnant patients (73/1559 vs. 6/723, $p < 0.001$). The risk of preterm labor is the highest in the first week after the surgery. That is why intravenous tocolytic and prophylactic antibiotic therapies prior to the surgical intervention are recommended [21]. Also, pregnancy loss was greater in case of appendectomy (2.6%) in comparison to other surgical interventions (1.2%) and rose to 10.9% in the event of coexisting peritonitis [22]. The risk of maternal or intrauterine death due to anesthesia or the surgery itself is believed to be lower than in the event of not undertaking action, therefore surgical treatment should not be delayed [23].

The case study presented by the authors was a rare case of appendicitis accompanied by a chronic illness, complications of which may mimic peritonitis, what presented an additional diagnostic difficulty. Symptoms suggesting ketoacidosis may include: excessive thirst, dryness in the mouth, polyuria, general weakness, torpor, consciousness disorders (including coma), dizziness, headaches, nausea, emesis, abdominal pain. Ketoacidosis in diabetic patients may have different clinical manifestations – cardiovascular collapse, renal failure, pseudopleuritis sicca or pseudoperitonitis diabetica.

The patient was urgently sent to the referral center due to ambiguous clinical picture resulting from long-term type 1 diabetes in the second trimester of pregnancy. At first she was suspected of metabolic decompensation and developing ketoacidosis – a life-threatening condition for the fetus and the mother should proper treatment be delayed. Therefore, the first line of treatment included blood gases, correction of insulin therapy and rehydration. After normal results of gasometry and no improvement in the overall condition of the patient, as well as exclusion of other reasons of peritoneal irritation, a decision was made to perform a reconnaissance laparotomy. The decision was particularly difficult as in case of this patient, apart from risk factors present during every emergency intervention in pregnancy, it was necessary to maintain normoglycemia in peri- and postoperative conditions. In the event of laparotomy performed due to appendicitis in pregnancy, the management is largely dependent on the week of gestation and may be combined with possible simultaneous induction of labor. The option was not possible in the case described due to early gestational age of the baby.

It is worth mentioning that even correct diagnosis of appendicitis and proper surgical management do not automatically reduce the risk of ketoacidosis as the result of sudden type 1 diabetes decompensation in reaction to acute inflammation. In such situation the direct risk of maternal and fetal life remains. Thus, maintaining glycemia in ranges as safe for the fetus as possible was the priority in post-operative treatment. Glycemia within reference ranges for pregnancy would have been ideal but to it was difficult due to stress, bed rest, strict diet followed by light diet which cannot include products beneficial for diabetic patients (with low glycemic index).

The natural inflammatory reaction of the body to the surgical treatment and the necessity of intravenous tocolytic treatment (corticosteroids for lung maturation were not administered due to early gestational week) constituted an additional factor hindering rapid metabolic stabilization in case of our patient. Therefore, the basis of the treatment was continuous infusion of rapid-acting insulin in a pump via a separate venous access site which allowed precise control over the flow in order to maintain normoglycemia and simultaneous administration of both, medicines impairing glucose tolerance as well as glucose in the amount sufficient for an increased energetic demand due to intensified catabolism after the surgery.

As the patient becomes mobile again and returns to regular diet, it is important to go back to the insulin therapy followed before the surgery and to adjust current doses of insulin. In our patient the HbA_{1c} at 30 weeks of gestation was 5.9%, what confirmed the efficiency of the post-operative treatment – return to normal glycemia levels and maintaining metabolic stability.

Yet another proof of maintaining long-term normoglycemia in the presented case is the correct for his age and sex/gender weight of the newborn, despite risk factor for worse neonatal outcome such as long-term type 1 diabetes, unplanned pregnancy, obesity (BMI before pregnancy 27.9 kg/m²) [24]. What is more, recurrent urinary tract infection and renal colic further deteriorated metabolic stability in case of our patient.

When presenting the clinical situation, the authors wish to emphasize that aggressive hypoglycemic treatment in acute hyperglycemia due to unknown causes in pregnant patients should immediately be introduced at the hospital they are first admitted. Rehydration, monitoring of glycemia and *iv* insulin infusion (if possible, in an infusion pump) is possible in any hospital and should be initiated as soon as possible if a pregnant patient presents with increasing hyperglycemia despite her own attempts to correct the doses of insulin (suggested plans of *iv* insulin infusion are presented in tables 1 and 2).

Further, more detailed diagnosis of hyperglycemia causes may and should be carried out in referral centers. However, it is the local hospital responsibility to initiate treatment and maintain values as close to the reference ranges as possible until the patient is transferred to the referral center. Current recommendations regarding management of pregnancy complicated with diabetes are available in the June issue of Ginekologia Polska [25].

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