Familial mediterranean fever: a diagnostic challenge in pregnancy

Ailevi akdeniz ateşi: gebelikteki tanısal güçlük"

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Abstract

Familial Mediterranean Fever (FMF) is an autosomal recessive disease which is characterized by recurrent, self-limiting, short attacks of serositis while abdominal pain is the most common symptom . The underlying clinical and pathological picture is that of acute peritonitis. These abdominal signs are often so striking that they mimic an acute abdominal calamity suggesting several possible gastrointestinal, gynecologic or urologic diagnoses. Diagnosis of acute abdomen in pregnancy also remains one of the most challenging conditions as the physiological consequence of pregnancy and nonspecific laboratory parameters. A limited number of studies addressed FMF in pregnancy and none of them mentioned the diagnostic challenging of FMF during pregnancy because the patients had al been diagnosed previously. In this paper , we discussed a 20 year old, gravida 1, parity 0 patient whose twin pregnancy wash complicated by an acute abdominal condition after amniocentesis and the difficulties of making the diagnosis of FMF with the complications during this diagnostic period in pregnancy.

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Özet

Ailevi Akdeniz Ateşi (AAA) en yaygın belirtisi karın ağrısı olan; tekrarlayıcı, kendi kendini sınırlayan, kısa serozit ataklarıyla karakterize, otozomal resesif geçişli bir hastalıktır. Altta yatan klinik ve patolojik görünüm akut peritonitle uyumludur. Bu batın bulguları bazen o kadar dikkat çekici bir duruma gelir ki, bazı gastrointestinal, jinekolojik ve ürolojik tanıları düşündüren akut karın tablosunu taklit eder. Gebelik sırasında akut karın tanısı koymak, gebeliğin fizyolojik sonuçlarına ve spesifik olmayan laboratuvar parametrelere bağlı olarak en zor durumlardan biridir. Gebelikte AAA ile ilgili sınırlı sayıda çalışma mevcuttur ve hiçbirinde AAA' nin gebelik sürecindeki tanısal zorluğundan bahsedilmemiştir, çünkü hepsi de gebelikten önce AAA tanısı almışlardır. Bu yazıda biz, 20 yaşında, gravida 1, parite 0 bir hastada amniosentez sonrasında akut karın tablosunu taklit ederek ikiz bir gebeliği komplike eden AAA' nin gebelik sürecinde tanısının konulmasındaki zorlukları ve bu tanısal süreçte meydana gelen komplikasyonları tartıştık

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Introduction

Familial Mediterranean Fever (FMF) is an inherited, recessively transmitted inflammatory condition usually occurring in populations of Jewish, Armenian, Arabic, and Turkish ancestry (1). The disease is characterized by recurrent, self-limiting, short attacks of serositis (peritonitis, pleuritis or arthritis), fever and erysipelas-like skin lesions along with a marked increase in acute phase reactants. Abdominal pain is generally the main manifestation of this disease. The underlying clinical and pathological picture is that of acute peritonitis. The pain may originate from a part of the abdomen but quickly becomes generalized. These abdominal signs are often so striking that they mimic an acute abdominal calamity suggesting several possible diagnoses such as appendicitis, gallbladder disease, acute pancreatitis, porphyria, recurrent small bowel obstruction and chronic inflammatory processes of the intestine (e.g. Crohn's disease).

The incidence of acute abdomen during pregnancy is 1 in 500–635 pregnancies (2, 3). Diagnosis of acute abdomen in pregnancy remains one of the most challenging conditions and therapeutic dilemmas today. As a physiologic consequence of pregnancy, the laboratory parameters are nonspecific and often altered. The most common cause of acute abdomen in pregnancy is acute appendicitis, but almost all causes of acute abdomen can manifest during pregnancy (4). In the literature search we did not detect FMF as a cause of acute abdomen during pregnancy. However, a limited number of studies (5-7) addressed FMF in pregnancy, but they were all previously diagnosed patients and none of them mentioned the diagnostic challenge of FMF during pregnancy. In this paper, we discussed the difficulties of making the diagnosis of FMF during pregnancy which complicated twin pregnancy by mimicking an acute abdominal condition after amniocentesis.

Case report

A 20 year old gravida 1, parity 0 patient referred to our clinic as a result of a spontaneous twin pregnancy of 6 weeks duration according to the last menstruation date. As the patient had a family history of Down's syndrome, they insisted on

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an amniocentesis being performed. Amniocentesis was performed at 18 weeks 4 days of gestational age and revealed a normal karyotype. The patient presented at the hospital suffering from abdominal pain, nausea and vomiting 4 days after amniocentesis. An ultrasound examination revealed the existence of a 19-week-old twin fetus with no grossly visible anomaly. On examination, the patient demonstrated abdominal rebound tenderness on the lower quadrant, signaling peritoneal irritation. Initially the pain was localized but quickly became generalized. She had no fever and laboratory findings were normal except for a high level of C-reactive protein (CRP) of about 48.3 mg/l (0-8 mg/l), whereas white blood count was 13200/mm^3 (3.6-9.6/mm^3). On the second day of follow-up, the patient complained of a fever of 38.5°C and abdominal pain again. The patient was consulted in the Department of General Surgery and acute surgical pathology was eliminated. As the clinics and laboratory findings of the patient were compatible with chorioamnionitis, antibiotherapy (Ampicillin 2 g i.v. loading dose followed by 1 g i.v. every 6 hr) was initiated. A second antibiotic treatment (Clindamycin 900 mg i.v. every 8 hr) was added as a result of the continuation of fever and increasing level of CRP (120 mg/l). Uterine contractions were detected by external cardiotocography, so indomethacin (Endol 100 mg rectal loading dose followed by 25 mg oral every 6 hr during 2 days) therapy was started. The patient was clearly informed that chorioamnionitis is one of the reasons of termination in pregnancy but she refused it even she was also informed about septisemic complications and she wanted to be discharged because the symptoms were ended after antibiotherapy. So she was discharged on the fifth day with oral antibiotherapy.

On the 20 weeks and 5 days of her pregnancy, the patient presented again suffering from the same symptoms and fever (38.5°C). Vaginal examination was normal. An abdominal ultrasonographic finding of a heterogeneous, vascularized, nonmobile cystic mass lesion observed in the right lower quadrant was suggestive of an abscess or a plastron formation. After consultation with General Surgery Department, laparotomy was agreed on for appendectomy. Fibrinoid adhesions all over the abdomen and non- inflammatory appendix were noted during laparotomy. Consultation was made with the Department of Internal Medicine on the fifth postoperative day due to suspicion of FMF as one of the most probable diagnoses

A new abdominal pain attack occurred on the 23 weeks plus 4 days of her pregnancy, colchicine therapy (1 mg/day) was initiated depending on the safety of it in pregnancy and no more attacks occurred during pregnancy. The patient was hospitalized on the 34 weeks plus 2 days of gestation with the diagnosis of preterm labor, and caesarian section delivery was performed as the first fetus was in breech presentation and the second in cephalic presentation. Genetic analysis of the patient was performed and Mediterranean Fever gene (MEFV) gene was found to be positive in the postpartum 6th week.

Discussion

This is the first report of FMF presenting as a diagnostic challenge in a mid-trimester patient with spontaneous twin pregnancy. It also emphasizes the importance of careful history taking to avoid unnecessary surgical interventions in acute abdomen during pregnancy. Despite advances in medical technology, diagnosis of acute abdomen during pregnancy is still inaccurate. Certain anatomic and physiologic changes specific to pregnancy may make the cause of the pain difficult to ascertain. Laboratory parameters also are nonspecific and often altered as a physiological consequence of pregnancy. The most common cause of the acute abdomen in pregnancy is acute appendicitis, but almost all causes of acute abdomen can manifest during pregnancy. Differential diagnosis should include FMF, which is characterized by recurrent attacks of fever and inflammation of serous membranes (8). Abdominal pain is the main manifestation of this disease. Although the majority of patients have a random pattern of attacks, without a clear precipitating factor, it has been observed that trauma, exertion, cold exposure, emotional stress and eating a fatty meal may precede attacks (9, 10). In our patient, FMF attacks occurred 4 times during pregnancy and the first attack started after amniocentesis. Therefore, the emotional and physical stress of amniocentesis may have precipitated the first attacks. There are contradictory reports relating FMF attacks during pregnancy; some patients may experience complete symptomatic remission but others may have attacks even more frequently. Acute phase reactants such as CRP, sedimentation rate and fibrinogen levels increase during an acute attack. An elevated white blood cell count with an increase in immature forms is seen. These laboratory findings are not diagnostic but when present they serve to support the diagnosis.

The reported incidence of chorioamnionitis following amniocentesis in the literature is 0.1%. Uterine tenderness, fever and high levels of infection parameters are the most important diagnostic criteria in the diagnosis of chorioamnionitis. Although we performed the procedure after an only one attempt in the midline of the abdomen 2 cm below the umblicus under sterile conditions, laboratory findings and symptoms led us to suspect corioamnionitis. But the continuation of fever and the changing characteristics of abdominal pain after antibiotherapy led us to a laparotomy to establish the pathology and to settle the symptoms. On laparotomy, non-inflammatory appendicitis and prevalent fibrinoid adhesions led us to suspect FMF. Then the patient mentioned abdominal pain attacks also before pregnancy when a more detailed medical history was obtained from her. Based on these findings FMF was the third probable diagnosis for our patient. Genetic analysis also confirmed our diagnosis of FMF.

In gynecological practice, FMF is usually not easily recognized. Patients often undergo exhaustive investigations and remain undiagnosed for years. Their histories often include multiple laparoscopies and laparotomies. Although genetic diagnostics are currently available (11), the diagnosis of FMF is still highly dependent on a clinical suspicion. Detailed medical history and the surgical finding during laparotomy helped us to diagnose her as FMF. To the best of our knowledge this is the first report handling the diagnostic challenge of FMF during pregnancy. This case also emphasizes the importance of careful anamnesis to avoid unnecessary surgical interventions in acute abdomen during pregnancy.

In conclusion, non-obstetric as well as obstetric reasons should be kept in mind in the differential diagnosis of acute abdomen during pregnancy. FMF should be remembered in young patients with recurrent attacks of abdominal pain and fever to avoid the hazard of misdiagnosis and to prevent unnecessary emergency operations during pregnancy.

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