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A prolonged gestational intrahepatic cholestasis: A case report

Gebeliğe bağlı uzamış intrahepatik kolestaz: Olgu sunumu

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Gestational intrahepatic cholestasis, characterized by generalized pruritus and biochemical changes of cholestasis, usually occurs in the third trimester of pregnancy, persists until delivery and resolves spontaneously within the initial four weeks of the puerperium. The incidence is dependent on genetic basis, environmental factors and geographical location. We report the case of a patient with gestational intrahepatic cholestasis with an extraordinary clinical course that extended to the 82nd week postpartum.

Key words: Gestational intrahepatic cholestasis, etiology, treatment

Gestasyonel intrahepatik kolestaz, yaygın kaşıntı ve kolestaza işaret eden biyokimyasal değişikliklerle karakterize bir antite olup, sıklıkla gebeliğin 3. trimesterde ortaya çıkar, doğuma kadar devam eder ve puerperyumun ilk 4. haftasında kendiliğinden geçer. İnsidansı etkileyen başlıca unsurlar kalıtım, çevresel faktörler ve coğrafi yerleşimdir. Bu yazıda, postpartum 82. haftaya kadar süren, sıradışı uzamış bir gestasyonel intrahepatik kolestaz olgusu rapor edilmiştir.

Anahtar kelimeler: Gestasyonel intrahepatik kolestaz, etyoloji, tedavi

INTRODUCTION

Chronic intrahepatic cholestasis is the most prevalent disease particular to pregnancy, known as GIHC (gestational intrahepatic cholestasis), and is characterized by itching and findings of cholestasis in the biochemical studies. It usually occurs in the last trimester, persists until delivery, and resolves on its own accord. The incidence varies depending on genetic make-up, geography, and environmental factors. The incidence is 1-2 in every 100 pregnant women in the populations with relatively lower risk, while it is 10 times higher in the Scandinavian countries, Poland, and Chile (1, 2). The incidence rate of the disease in Turkey is unknown.

CASE REPORT

A 36-year-old pregnant patient applied to the Dermatology Clinic of our hospital with the complaint of pruritus in February 2002. Laboratory studies disclosed the following values: AST: 47 U/L, ALT: 39 U/L, GGT: 114 U/L, ALP: 526 U/L, total bilirubin: 1.5 mg/dl, total cholesterol: 369 mg/dl and triglyceride: 334 mg/dl. The patient was then referred to the gastroenterology outpatient clinic. Her history revealed a complaint of pruritus for the last five months, corresponding to the 29-30th weeks of pregnancy.

Patient history revealed that she had been on an ovulation induction treatment for the last 5-6 years at certain intervals and had acquired her pregnancy by in-vitro fertilization and embryo transfer (IVF-ET) method. Her familial history had no specificity.

Her physical examination was normal. Complete blood count, erythrocyte sedimentation rate, prothrombin time, thyroid function tests, and serum albumin, iron and ferritin levels were within normal limits. All viral (HbsAg, antiHBs, antiHbc Ig, anti-HCV) and autoimmune markers [antinuclear antibodies (ANA), anti-smooth muscle

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antibodies (SMA), liver kidney microsome antibodies type 1 (LKM1A), antimitochondrial antibodies (AMA) type 2] and p ANCA were negative. Abdominal ultrasonography (USG) and magnetic resonance cholangiopancreaticography (MRCP) revealed no pathology. The patient had a cesarean delivery in the 34th week of her pregnancy. However, even 3-3.5 months after delivery, her complaints persisted. Results of hepatic function tests of the patient in the follow–up period are listed in Table 1.

The histopathological examination of the liver biopsy, applied in October 2002, confirmed the diagnosis of chronic intrahepatic cholestasis. UDCA treatment at a dose of 15 mg/dl was then started. The patient was followed up regularly and at the 86th week hepatic function tests were in normal limits.

Table 1. Laboratory values of the patient after delivery

Time	AST U/L	ALT U/L	GGT U/L	ALP U/L	TB mg/dl	Triglycerides mg/dl	Cholesterol mg/dl
15th week	47	39	114	526	1.5	334	369
19th week	36	120	608	586	1		
42nd week	38	47	80	500	0.91	254	267
50th week*	60	91	451	476	0.87	225	246
65th week	23	25	148	262	0.9		
82nd week	25	28	137	347	1.2		

*UDCA treatment was started, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, GGT: gamma-glutamyl transpeptidase, ALP: Alkaline phosphatase, TB: Total bilirubin

DISCUSSION

The diagnosis of GIHC is essentially based on the clinical findings. Widespread pruritus not accompanied by dermatological lesions in a pregnant woman is suggestive of GIHC. Through laboratory examinations, the pathologies such as viral hepatitis, chronic hepatitis, gallbladder stone, drug reactions, primary biliary cirrhosis, and sclerosing cholangitis can be ruled out; thus rendering a definitive diagnosis. All symptoms and findings disappear in a maximum of four weeks after the delivery and are never seen in any period of life other than in pregnancy. This is a very valuable criterion but evaluated relatively later in the process of diagnosis (3). Similarly, in our case, pruritus was the primary complaint. The diagnoses of viral and chronic hepatitis were ruled out by the evaluation of viral and autoimmune markers. Since the results of abdominal USG, MRCP and pANCA were normal, pathologies such as gallbladder stones and primary sclerosing cholangitis were also ruled out. Cholestasis of pregnancy is generally a self-limiting condition that occurs in the last trimester and disappears within 1-2 weeks after delivery. In our case, the complaints of the patient persisted even in the postpartum 82nd week, which was indicative of an unusual clinical progression. Olsson et al. (4) reported cases of prolonged intrahepatic cholestasis persisting until the 35th and even 40th week. In Sherlock's (5) view, prolonged GIHC cases are actually cases of primary biliary cirrhosis. In our case, AMA M2 evaluation yielded negative results, and the findings of the liver biopsy were compatible with those in chronic cholestasis. Therefore, the differential diagnosis of primary biliary cirrhosis was ruled out. Since our patient had conceived via IVF-ET method and had twins, the literature was also reviewed in this respect. Koivurova et al. (6) reported that the incidence of intrahepatic cholestasis for those whose conceptions were through supportive reproduction techniques was higher than among those with spontaneous pregnancy.

Gestational intrahepatic cholestasis requires a symptomatic treatment. The patients usually have various responses to different agents used in the treatment (7). Despite improvement in the pruritus complaint of our patient following treatment with UDCA after eight weeks, GGT and ALP levels remained high and returned to normal limits later.

In conclusion, GIHC usually resolves within the first two days or two weeks of delivery. However, it may rarely persist as long as 35-43 weeks. Our case was unique because of prolonged intrahepatic cholestasis until the 82nd week after delivery.

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