Case Report

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Intrahepatic Cholestasis of Pregnancy: Case Report and Review of the Literature

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Abstract

Gestational cholestasis of pregnancy is a dermatosis of pregnancy clinically characterized by the appearance, more frequent in the third trimester of pregnancy of pruritus, predominantly palmoplantar and nocturnal. Organically, it is associated with elevation of cholestasis enzymes and, especially, bile acids. Given its suspicion, and due to the risk of fetal involvement, maternal-fetal evaluation by an obstetrician is essential and initiation of treatment with ursodeoxycholic acid. We present the clinical case and a narrative review of this entity. Knowledge of it is essential for every doctor since its early diagnosis and treatment allows less fetal morbidity and mortality.

Keywords: Bile Acids, Cholestasis, Pregnancy, Pruritus.

Case Report

A 36-year-old woman with no relevant personal history presented to the dermatology emergency room. Born in Colombia, the patient was a 39-week pregnant woman who consulted for generalized pruritus of three days of evolution, predominantly nocturnal and palmoplantar accentuation. With a sudden onset, she did not associate it with any trigger and there was no family environment either. The rest of the pregnancy had gone without any type of complication. As antecedent, she reported that in her first pregnancy, during the last few weeks, she presented a similar itch, but of less intensity, and that it subsided spontaneously after delivery. On examination, excoriated papules can be seen on the anterior side of the trunk, suggestive of scratching lesions (black arrows in panel A). Likewise, erythema was observed in the palmar region of both hands (panel B). No other skin or mucosal lesions were noted.

Due to the suspicion of intrahepatic cholestasis of pregnancy, an analysis was requested, which revealed an elevation of cytolysis liver enzymes and, especially, of alkaline phosphatase (1,500 U/L, with a normal range of 40-150 U/L). and bile acids (105.3 µmol/L, with a normal range of 1.3-9 µmol/L). An obstetric evaluation was performed, confirming good fetal status, and treatment was started with ursodeoxycholic acid at a dose of 150mg/8 hours and dexchlorpheniramine at a dose of 2mg/8 hours. Subsequently, in a week, given the clinical-analytical data and the presence of a full-term pregnancy, the Obstetrics decided to terminate the pregnancy. The delivery was normal, with a totally healthy neonate weighing 3,450g. Fetal follow-up at 3 months was completely normal. Similarly, maternal symptoms subsided 2-3 days after delivery, with no subsequent recurrence in the following 3 months.

Review of the Literature

Pregnancy is a physiological situation with implications for multiple body systems, including the skin. Most of the changes that occur in the skin during pregnancy are physiological and among them we have an increase in hyperpigmentation (black line, areolar, melasma, nevus, vulvar melanosis, etc), an increase in stretch marks, changes in the hair (such as postpartum telogen effluvium), nails (fragility, longitudinal melanonychia, etc), vascular (telangiectasias, varicosities, lobular capillary hemangiomas, etc), as well as in the different eccrine glands (increased sweat and apocrine and sebaceous production). Likewise, immunological changes appear, pregnancy being a situation of "immunoprivilege", which aims to protect the fetus from autoimmune attack (hence, for example, the change of the T helper response to Th2) [1]. In addition to these physiological changes, approximately 50% of pregnant women experience exacerbations of previous dermatoses (psoriasis, atopic dermatitis, lupus, systemic sclerosis, etc.) and, in addition, we have the so-called "pregnancy-specific dermatoses", typical entities of this period

of life: pemphigoid gestationis, polymorphic eruption of pregnancy, atopic eruption of pregnancy, and intrahepatic cholestasis of pregnancy.

These entities are important, both for their symptoms and affectation of the quality of life of parturients, and for the possible risk of fetal involvement, which has been documented in both pemphigoid gestationis and intrahepatic cholestasis of pregnancy [2]. Intrahepatic cholestasis of pregnancy or cholestasis gravidarum is a pregnancy-specific dermatosis characterized by the appearance of pruritus with possible liver involvement. It is a rare entity, with an estimated prevalence between 1-2.5% and more frequent in South America. There is a tendency to family aggregation. Its etiopathogenesis is multifactorial, different factors have been implicated, including genetics (especially through the ABCB4 gene, involved in bile canalicular transport), the predominance of estrogenic hormones or environmental factors (vitamin D or selenium deficiency). All of this generates a situation of retention of cholestasis enzymes, which cause the symptoms, both at the cutaneous, hepatic, and systemic levels [3].

The characteristic symptoms are based on the appearance of pruritus in the third trimester of pregnancy, predominantly palmoplantar and nocturnal. This clinic is aggravated in successive pregnancies. Up to 25% of patients present with jaundice. Right upper quadrant pain, hepatomegaly, nausea, or vomiting are rare3. Dermatologically, the most frequent is not finding skin lesions. However, in some cases we find icteric tint, palmoplantar erythema or scratching lesions [3]. In the differential diagnosis, it is important to differentiate it from other causes of pruritus in pregnancy, such as atopic eruption of pregnancy, polymorphous eruption, pemphigoid gestationis, scabies, urticaria, drug eruptions, or allergic processes. Especially important, due to its prognostic implications, is to rule out acute fatty liver of pregnancy, which produces a similar clinical picture, but usually with persistent nausea and vomiting and with an analysis that highlights coagulopathy [3,4].

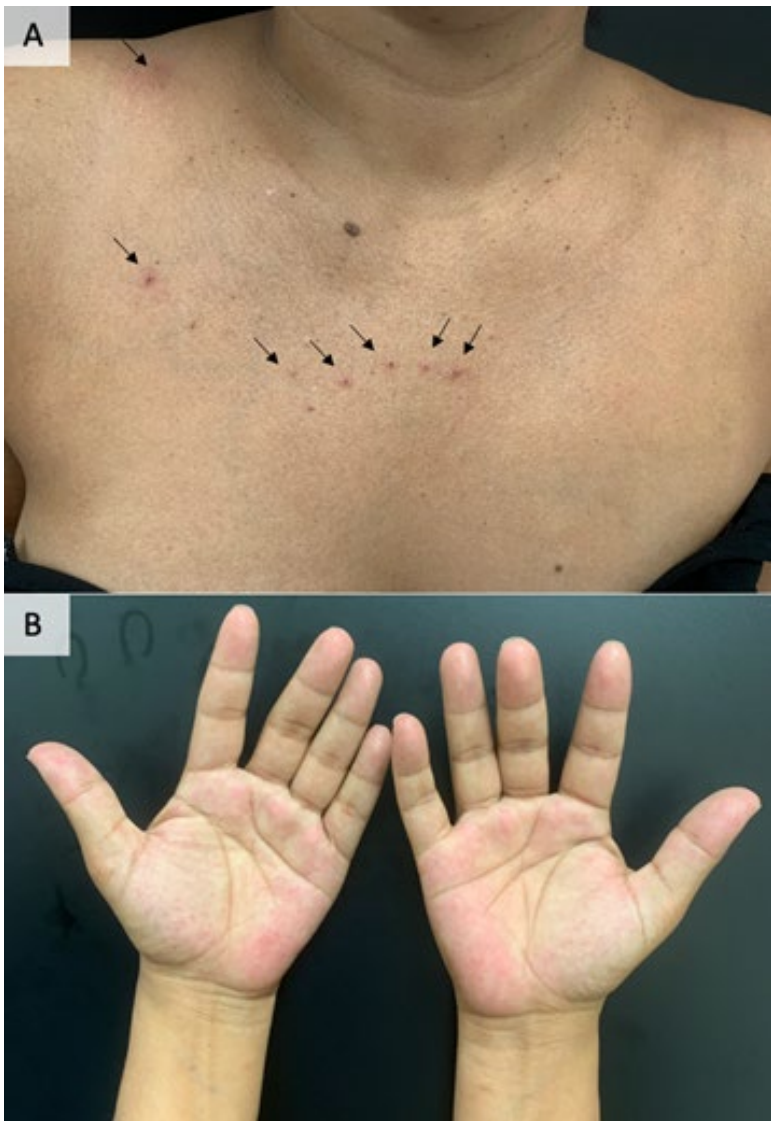
In addition to the clinic, in the diagnosis it is necessary to establish a correct fetal evaluation by Obstetrics and a blood test, which highlights the elevation of bilirubin and liver enzymes of cholestasis and, especially, the elevation of bile acids. A value greater than 10 µmol/L is highly suggestive of cholestasis of pregnancy, although its negativity does not exclude the diagnosis [4]. The importance of cholestasis gravidarum lies in its possible fetal involvement. A recent review of perinatal outcomes in patients with cholestasis gravidarum reported fetal involvement in 152 of 4128 patients (3.6%) [5]. Most of them (92%) presented mild symptoms, although 2% of intrauterine deaths were recorded and 10% of newborns required positive pressure resuscitation at birth. A correlation was observed between fetal severity and maternal bile acid levels.

Given the suspicion of intrahepatic cholestasis, early referral to an obstetrics service is essential for fetal assessment and early initiation of ursodeoxycholic acid at a dose of 15mg/kg/day. This treatment should be started empirically, without waiting for the analytical result, since early treatment improves perinatal outcomes. Regarding the termination of pregnancy, traditionally, the management of these patients was based on the induction of labor at 37 weeks of gestation. However, more current studies and protocols defend the stratification of these patients. The most widely used protocol in Spain (with the participation of the Clìnic and Sant Joan de Deu hospitals, both in Barcelona) divides patients with cholestasis gravidarum into three groups [6]. The first of these would be made up of patients with good clinical control and bile acids < 40 µmol/L. In this subgroup, pregnancy could be terminated from 40 weeks.

In the intermediate term, we would have a second subgroup of patients, made up of those with bile acids between 40 and 100 µmol/L, those with poor clinical control despite treatment, those with laboratory worsening, or those with a history of fetal death due to cholestasis. In this subgroup, termination at 40 weeks of pregnancy is advocated. Finally, a third group of patients with bile acids >100 µmol/L is recommended for completion before week 37, after fetal maturation with corticosteroids [6]. After delivery, the maternal symptoms usually resolve in the following days. No subsequent analytical test is necessary in the parturient. It is important to inform patients of the risk of recurrence in subsequent pregnancies of up to 40-60%, often with more severe symptoms [2, 6]. In conclusion, we present a clinical case and a review of the literature on gestational cholestasis of pregnancy. Knowledge of this entity is essential for every dermatologist and obstetrician since its non-recognition can lead to fatal perinatal outcomes.

Figure Legend

Skin lesions at the time of consultation: In panel A, excoriated papules can be seen in the anterior thorax (black arrows), corresponding to lesions caused by scratching. In panel B, bilateral palmar erythema can be seen.



Author Contributions

1. Miguel Mansilla-Polo, Blanca Novillo-Del Álamo and Daniel Martín-Torregrosa managed clinical treatment and procedures, contributing to the development of this paper.
2. Carlos Abril-Pérez and Mónica Pozuelo-Ruíz directed the writing of the manuscript and follow-up of the patient.
3. Ignacio Torres-Navarro and Rafael Botella-Estrada supervised the work.

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