Profilaktik tibbiyot va salomatlik – Профилактическая медицина и здоровье – Preventive Medicine and Health
Journal home page:
https://inscience.uz/index.php/preventive-medicine

Thrombotic storm: clinical profile and differential diagnosis of catastrophic antiphospholipid syndrome in pregnancy

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ARTICLE INFO

Article history:
Received July 2025
Received in revised form
10 July 2025
Accepted 25 July 2025
Available online
15 August 2025

Keywords:
catastrophic antiphospholipid syndrome, pregnancy, thrombotic microangiopathy, diagnosis, D-dimer, antiphospholipid antibodies, differential diagnosis.

ABSTRACT

The objective is to identify and systematize the characteristic clinical, laboratory, and instrumental features of catastrophic antiphospholipid syndrome (CAPS) in pregnant women, thereby improving its timely diagnosis and differentiation from other thrombotic microangiopathies (TMAs).

Materials and Methods: A cohort study of 12 patients diagnosed with CAPS that developed during pregnancy was conducted. A detailed analysis of the clinical picture, obstetric and perinatal outcomes, biochemical and hemostatic markers, as well as dopplerometry data was performed.

Results: It was established that the clinical profile of CAPS is characterized by the rapid development of multi-organ failure with predominant kidney involvement (median creatinine 74.90 μmol/L). The syndrome is associated with extremely adverse perinatal outcomes.

Conclusion: CAPS in pregnancy has a unique clinical and laboratory pattern, the key elements of which are a triad: acute kidney injury, an exceedingly high D-dimer level, and a confirmed high titer of aPL. The identification of this triad is crucial for differential diagnosis and the immediate initiation of life-saving therapy.

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DOI: https://doi.org/10.47689/2181-3663-vol4-iss1-pp66-70

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Trombotik to‘fon: homiladorlikda katastrofik antifosfolipid sindromining klinik manzarasi va differensial diagnostikasi

Kalit so‘zlar:
katastrofik antifosfolipid sindrom,
homiladorlik,
trombotik mikroangiopatiya,
diagnostika,
D-dimer,
antifosfolipid antitanachalari,
differensial diagnostika.

ANNOTATSIYA

Maqsad: Homilador ayollarda katastrofik antifosfolipid sindromining (KAFS) o‘z vaqtida tashxis qo‘yishni va uni boshqa trombotik mikroangiopatiyalardan (TMA) farqlashni yaxshilash uchun unga xos bo‘lgan klinik, laborator va instrumental belgilarni aniqlash va tizimlashtirish.Materiallar va usullar: Homiladorlik davrida rivojlangan KAFS tashxisi qo‘yilgan 12 nafar bemordan iborat kohort tadqiqoti o‘tkazildi. Klinik manzara, akusherlik va perinatal oqibatlar, biokimyoviy va gemostaziologik markerlar, shuningdek, dopplerometriya ma’lumotlari batafsil tahlil qilindi.

Natijalar: KAFSning klinik manzarasi buyraklarning ustun darajada zararlanishi (kreatinin medianasi 74,90 mkmol/l) bilan kechadigan poliorgan yetishmovchiligining jadal rivojlanishi bilan tavsiflanishi aniqlandi. Sindrom o‘ta noqulay perinatal oqibatlar bilan bog‘liq. Laborator profil D-dimerning o‘ta yuqori darajasi (mediana 1531,50 ng/ml), antifosfolipid antitanachalarining (aFL) maksimal titrlari va mikroangiopatik gemolitik anemiya belgilari bilan ajralib turadi.

Xulosa: Homiladorlikdagi KAFS o‘ziga xos noyob klinik-laborator naqshga (patternga) ega bo‘lib, uning asosiy elementlari quyidagi triadadan iborat: o‘tkir buyrak shikastlanishi, D-dimerning haddan tashqari yuqori darajasi va aFLning tasdiqlangan yuqori titri. Ushbu triadaning aniqlanishi differensial diagnostika va hayotni saqlab qoluvchi terapiyani zudlik bilan boshlash uchun hal qiluvchi ahamiyatga ega.

Тромботический шторм: клинический портрет и дифференциальная диагностика катастрофического антифосфолипидного синдрома при беременности

Ключевые слова:
катастрофический антифосфолипидный синдром,
беременность,
тромботическая микроангиопатия,
диагностика,
D-димер,
антифосфолипидные антитела,
дифференциальная диагностика.

АННОТАЦИЯ

Цель: Определить и систематизировать характерные клинические, лабораторные и инструментальные признаки катастрофического антифосфолипидного синдрома (КАФС) у беременных для улучшения его своевременной диагностики и дифференциации от других тромботических микроангиопатий (ТМА).

Материалы и методы: Проведено исследование когорты из 12 пациенток с диагнозом КАФС, развившимся во время беременности. Проведен детальный анализ клинической картины, акушерских и перинатальных исходов, биохимических и гемостазиологических маркеров, а также данных допплерометрии.

Результаты: Установлено, что клинический портрет КАФС характеризуется стремительным развитием полиорганной недостаточности с преимущественным поражением почек (медиана креатинина 74,90 мкмоль/л). Синдром ассоциирован с крайне неблагоприятными перинатальными исходами.

Заключение: КАФС при беременности имеет уникальный клинико-лабораторный паттерн, ключевыми элементами которого являются триада: острое почечное повреждение, запредельно высокий уровень D-димера и подтвержденный высокий титр аФЛ. Идентификация этой триады имеет решающее значение для дифференциальной диагностики и немедленного начала жизнеспасающей терапии.

INTRODUCTION

Catastrophic antiphospholipid syndrome (CAPS) is an obstetric emergency, comparable to a "thrombotic tsunami" that suddenly and devastatingly overwhelms the maternal and fetal systems. This pathology demands not just knowledge from clinicians, but a very high index of suspicion. The urgency of timely diagnosis is dictated by the extreme severity of the syndrome, with a mortality rate that can reach up to 50% even with modern management, and the necessity for immediate initiation of complex, multicomponent therapy [Asherson R.A., 2006; Sidorova I.S., 2020]. Any delay in diagnosis directly correlates with an increase in maternal and perinatal mortality.

LITERATURE REVIEW

Thrombotic microangiopathies (TMAs) represent a heterogeneous group of disorders that pose one of the most challenging diagnostic and therapeutic problems in modern obstetrics. The clinical presentation of TMAs, which includes thrombocytopenia, microangiopathic hemolytic anemia, and multi-organ dysfunction, can be similar across various pathologies such as severe preeclampsia/HELLP syndrome, thrombotic thrombocytopenic purpura (TTP), atypical hemolytic uremic syndrome (aHUS), and CAPS [Makatsariya A.D., 2018].

CAPS, first described by R.A. Asherson, is the rarest (<1% of all APS cases) but most fulminant form, characterized by rapid thrombosis of small-caliber vessels in three or more organs [Cervera R., 2017]. The main challenge lies in the differential diagnosis, as therapeutic approaches differ radically: while delivery is the cornerstone of management for HELLP syndrome, for CAPS, this is insufficient, and aggressive immunosuppressive and anticoagulant therapy is required. Identifying specific markers and clinical patterns of CAPS is a key priority.

Therefore, our study aimed to provide clinicians with a clear clinical and laboratory "portrait" of CAPS, based on the analysis of real clinical cases, to facilitate rapid and accurate decision-making in critical situations.

MATERIALS AND METHODS

An observational cohort study was conducted, which included 12 patients with CAPS that developed during pregnancy, verified according to international criteria. A comprehensive analysis was performed on medical history, clinical manifestations, and laboratory parameters (complete blood count, biochemical profile, coagulation profile

including D-dimer levels, quantitative measurement of all classes of antiphospholipid antibodies). Instrumental studies, including Doppler ultrasonography of the uteroplacental and fetal circulation, were also analyzed. Statistical analysis included the calculation of medians (Me) and interquartile ranges [Q1-Q3].

ANALYSIS AND RESULTS

The clinical picture of CAPS presented as a rapidly developing multi-organ catastrophe. A characteristic feature distinguishing it from other TMAs was the pattern of organ involvement. The primary target organ in the study group was the kidneys, which were convincingly confirmed by peak levels of creatinine (median 74.90 μmol/L) and urea (median 4.85 mmol/L), indicating the development of acute kidney injury (AKI).

Laboratory parameters were a precise reflection of the "thrombotic storm." The key marker was the D-dimer level, with values an order of magnitude higher than in other obstetric complications, reaching a median of 1531.50 ng/mL. This unprecedentedly high level indicated massive, uncontrolled activation of coagulation throughout the entire vascular bed.

The process was accompanied by moderate thrombocytopenia (median 180.5 x10^9/L) and anemia (median 110.0 g/L) due to the development of microangiopathic hemolytic anemia, which was also confirmed by high levels of lactate dehydrogenase (LDH) (median 284.50 U/L). The fundamental immune nature of the process was evidenced by extremely high titers of all classes of antiphospholipid antibodies.

The severity of the maternal condition inevitably affected the fetus. Across all key obstetric outcomes, the CAPS group demonstrated an extremely unfavorable pregnancy trajectory. The median gestational age at delivery in the CAPS group was 35.0 [31.00-36.00] weeks, which was statistically significantly lower compared to the control group (Me 39.0 [38.25-40.00] weeks; $p<0.001$).

This premature termination of pregnancy was necessitated by the uncontrolled progression of the pathology and the need to save the mother's life. A direct consequence was a significant reduction in neonatal anthropometric parameters. The median birth weight in the CAPS group was 1800.0 [1330.00-2112.50] g (vs. 3410.0 [3006.25-3747.50] g in the control group; $p<0.001$), and the median length was 43.5 [40.75-45.25] cm (vs. 53.0 [51.00-55.00] cm in the control group; $p<0.001$).

These critically low values are indicative of severe intrauterine growth restriction (IUGR) and the consequences of prematurity, caused by severe placental insufficiency and chronic hypoxia resulting from the systemic thrombotic process.

Parity analysis revealed a predominance of multiparous women in the CAPS group (83.3%, n=10). This may suggest that multiparity is not a protective factor in CAPS and that previous adverse outcomes may have been associated with undiagnosed APS.

Fetal distress was objectively confirmed by Doppler ultrasonography, which revealed significant blood flow abnormalities: the pulsatility index (PI) in the uterine arteries (median 1.44) and the umbilical artery (median 1.05) was significantly elevated, while in the fetal middle cerebral artery (MCA), it was compensatorily decreased (median 0.98), reflecting the "brain-sparing" phenomenon.

CONCLUSION AND RECOMMENDATIONS

Catastrophic antiphospholipid syndrome in pregnancy presents with a unique and recognizable clinical and laboratory profile. Its key elements comprise a diagnostic triad: acute kidney injury (AKI), extremely elevated D-dimer levels, and confirmed high titers of antiphospholipid antibodies. Recognition of this triad in a pregnant patient with rapid and unexplained deterioration is the key to establishing a correct diagnosis.

When a pregnant patient presents with a picture of thrombotic microangiopathy, a high index of suspicion for CAPS must be maintained, especially if the patient has a history of APS. Urgent evaluation of D-dimer levels, renal function, and antiphospholipid antibody status is paramount. If CAPS is suspected, a multidisciplinary team (obstetrician-gynecologist, intensivist, rheumatologist, hematologist, nephrologist) should be assembled immediately to develop a management plan.

Timely diagnosis, based on the presented clinical and laboratory profile, is the primary factor determining the possibility of saving the lives of both the mother and the child.

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