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Sneathia infections and adverse perinatal outcomes – short communication

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ABSTRACT

The influence of the maternal vaginal microbiome in vaginal birth is an important factor in the pathogenesis of early-onset neonatal sepsis. The incidence of Sneathia infection is hard to assess due to the difficulty in its detection, as special culture conditions are required. The laboratory methods used in its detection are based on molecular analysis. This emergent, anaerobic agent, by ascending from the female genital tract, can colonize and infect the amniotic fluid, fetal membranes, and placenta. Chorioamnionitis, neonatal sepsis, stillbirth, spontaneous premature labor, and preterm prelabour rupture of the membrane are some of the adverse reactions that can be associated with the presence of Sneathia. In conclusion, Sneathia infection, although underestimated due to its virulence, represents an increased risk of maternal-fetal infections, with the risk of developing a series of neonatal complications. The detection and treatment of this infection will contribute to a decrease in neonatal morbidity and mortality.

Keywords: Sneathia infection, chorioamnionitis, amniotic fluid colonization, bacterial vaginosis, microbiome, preterm birth, preterm prelabor rupture of membrane

INTRODUCTION

Intra-amniotic infection can occur through the ascent of germs belonging to the microbiota from the lower genital tract to the level of the amniotic cavity. This infectious process is frequently associated with obstetric complications. Studies in relation to hematogenous dissemination validate this pathogenic mechanism. Thus, after invasive procedures (amniocentesis) or by ascending the germs from the fallopian tubes into the peritoneal cavity, the germs identified in the cultures obtained from the amniotic fluid are similar to those from the vaginal microbiome. Clinical chorioamnionitis and preterm labor with intact or ruptured membranes have germs from the vaginal sphere as their starting point [1,2].

Identifying the germs from the cultures obtained from the amniotic fluid revealed that in 62.5% of the women, they were present in the vaginal microbiome. Furthermore, the cultures obtained from the amniotic fluid and vagina were frequently dominated by the presence of the following germs: Escherichia coli, Streptococcus agalactiae, and Ureaplasma urealyticum. Instead, in pregnant women with chorioamnionitis, the use of molecular sequencing methods of the 16S rRNA gene showed the following bacterial profile dominated by Sneathia, Escherichia, Ureaplasma, Streptococcus, Lactobacillus, Peptostreptococcus, and Gardnerella [2].

In recent years, special attention has been paid to infection with Sneathia spp. due to possible complications like septic abortion, preterm birth, chorioamnionitis, stillbirth, postpartum maternal sepsis, and neonatal sepsis [3].

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The maternal microbiome has several germs in its composition, including the bacterium Sneathia, which comes from the Leptotrichiaceae family, anaerobic, Gram-negative, similar to the stick, and can cause a series of maternal-fetal infections with an inauspicious prognosis. Initially, the genus Sneathia was classified in the genus Leptotrichia due to its similarity to the latter by sequencing the 16S rRNA gene [4]. Thus, in 2004, Leptotrichia amnionii was reclassified into Sneathia amnii, isolated from the amniotic fluid of a pregnant woman with acute chorioamnionitis and intrauterine fetal death [6]. This genus includes the species Sneathia amnii and Sneathia sanguinegens, located in the genital tract, gastrointestinal tract, and oral cavity [5]. Sneathia species were frequently discovered in patients with symptomatic bacterial vaginosis. The presence of this bacterium in the maternal microbiota is extremely variable, between 1 and 21% in pregnant women [5].

DNA sequencing procedures have identified these bacteria in cultures obtained from the genital tract, blood, and amniotic fluid [6]. In a study carried out in 2019, Eisenberg et al. proposed a new taxonomic description by replacing the term Sneathia amnii with Sneathia vaginalis sp. nov., isolated from cultures obtained from blood collected from patients with puerperal fever [4].

The studies carried out in recent years show a role in the continuous increase of Sneathia infection in the pathogenesis of bacterial vaginosis, chorioamnionitis, premature labor, PPROM, and stillbirth. Bacterial vaginosis has as its main mechanism of occurrence and progression the formation of the biofilm at the level of the vaginal mucosa. The virulence of this infection is defined by the ascent of the germs, their invasion, and fixation at the level of the fetal membranes, followed by a cytolytic process, as well as the response of the host's immune system [5]. The mechanisms by which the ascent to the uterus and subsequent intra-amniotic invasion are not yet elucidated. The hydrolysis of the mucus would determine a possible way of action of the Sneathia infection at the cervix by sialidase or by the process of red blood cell lysis and permeabilization of the trophoblast by the cytotoxic exotoxin produced by Sneathia amnii [7].

The structure of Sneathia amnii sp. nov. was identified within the Human Vaginal Microbiome Project, and classified as a representative of community status type IV (CST-IV). In addition, the association of Sneathia sanguinegens infection with clue cells and vaginal biofilm can define the virulence of this species [8].

Spontaneous induction of premature labor is defined as the occurrence of regular uterine contractions that will cause changes in the uterine cervix before 37 weeks, while PPROM is defined as spontaneous rupture of the membranes before the completion of 37 weeks and the initiation of contractions with an hour before. The diagnosis of chorioamnionitis in women with premature labor and intact membranes, which give birth prematurely, is perform from the amniotic fluid obtained by amniocentesis. Thus, in acute chorioamnionitis, infection with Sneathia spp. was detected either by the PCR technique or by genetic sequencing of 16S rRNA [9,10].

Studies have observed a clear link between the vaginal microbiota and preterm birth in Caucasian [11] and African-American women [12], by identifying colonies of Sneathia spp., S. amnii and S. sanguinegens. In the pathogenesis of preterm birth, the correlation between S. sanguinegens and the immunological biomarkers in the vaginal secretion (CCL2, CXCL10, CCL26, CCL22, and IL-16) was observed [13]. Also, in Sneathia infections, an increased inflammatory process was observed, and the association with vaginal cytokines IL-1α, IL-1β, and IL-8 [14].

The aggressiveness of the infection with Sneathia spp. could be realized by evaluating the signs of acute chorioamnionitis and funisitis in relation to the negative results of the pregnancy. Asymptomatic pregnant women with a short cervix evaluated by ultrasound and who gave birth at term presented a low virulence of infection with Sneathia spp. due to the lack of occurrence of the specific intra-amniotic inflammatory process [5]. The diagnosis of clinical chorioamnionitis requires the presence of the following criteria: maternal fever, odorous vaginal secretions, increased uterine sensitivity, fetal tachycardia, as well as leukocytosis with neutropenia. However, the detection rate of histologically proven intra-amniotic infection is low [15]. Clinical chorioamnionitis caused by polymicrobial infections presents a more severe inflammatory response than monomicrobial ones [10].

In the case of premature birth, the adverse effects of Sneathia sanguinegens infection were observed at the end of the second trimester and in the third trimester of pregnancy [16]. In support of this statement is the study by Wikström et al., which did not prove a connection between this infection and preterm birth, highlighted another diversity of bacteria such as Bifidobacterium breve, Enterococcus faecalis, Lactobacillus crispatus, Parvimonas micra, Cutibacterium acnes [17]. In contrast, in patients with previous preterm births, the study by Nelson et al. found that increased levels of up to 24 weeks of gestation of Sneathia, and Megasphaera phylotype 1, were associated with an increased risk of spontaneous preterm birth [18].

Sneathia and septic neonatal complications

In patients whose newborns developed early sepsis, Brown et al. showed the presence of cultures of Sneathia spp., Prevotella, Peptostreptococcus, Catonella spp., and Lactobacillus crispatus in their vaginal microbiome [19]. In a vaginal birth, the germs that colonize or infect the female genital tract and that are frequently involved in neonatal bacterial infection with early onset are Enterococcus, E. coli, Sneathia, and Globicatella [20].

The diagnosis of acute chorioamnionitis and funisitis is histopathological by analyzing the placenta and the umbilical cord. The suspicion of infection with Sneathia is considered in acute chorioamnionitis with intrauterine fetal death by analyzing the amniotic fluid and in abortions with increased septic risk by analyzing the maternal blood. Until now, the determining or favoring role of Sneathia infections in the pathogenesis of various obstetric and gynecological diseases could not be established [15].

Although microbial diversity decreases as pregnancy progresses, cases with diverse microbiota and bacterial vaginosis toward term have been observed [21].

Neonatal sepsis is identified in the first three months postpartum by bacteria in the blood (blood cultures) or the cerebrospinal fluid of the newborn. Thus, the appearance of premature newborns of fever and signs of respiratory condition requires cultures from blood, cerebrospinal fluid and stool to establish infection with Sneathia spp. [22,23].

On the 7th day postpartum, Jain et al. observed in the stool samples of infants born from pregnancies complicated with chorioamnionitis the following germs Sneathia, Fusobacteria, Enterobacteriaceae, or Mycoplasmataceae. Moreover, these infections present a high risk of sepsis and neonatal death [15].

In a study conducted in northeastern India by Utpala et al. regarding the bacterial etiology of neonatal meningitis, the following germs were isolated from the cerebrospinal fluid: Neisseria meningitidis serogroup Y8, Sneathia, and Globicatella. Antimicrobial treatment instituted with netilmicin for one week and piperacillin for 3 weeks improved the neurological prognosis of the newborn [20].

Septic maternal complications and therapeutic strategy

The proof that the infection with Sneathia sanguinegens and S. amnii can reach from the reproductive tract into the blood and other organs of the body, being responsible for intra and postpartum bacteremia in patients who developed fever, was achieved by performing blood cultures, using rRNA gene sequencing 16S [3,24]. Movassagh et al. found in a group of 99 pregnant women an increased prevalence in febrile patients of the genera Granulicatella, Fusobacterium, Anaerococcus, Streptococcus, Sneathia, Gemella, Mobiluncus, Clostridium, and Veillonella and of the genera Lactobacillus, Aerococcus, Acinetobacter, and Prevotella in afebrile women [25].

Sneathia was the second genus after Lactobacillus, discovered in the vaginal microbiota during labor [25]. Little data is known in the literature about the treatment of this infection. Oral administration of metronidazole in pregnant women with Sneathia bacterial vaginosis was superior to vaginal administration [26]. Another option would be the oral administration of tinidazole monotherapy or in combination with a probiotic [27]. Moreover, patients with bacterial vaginosis treated with metronidazole may be more likely to achieve long-term remission due to increased susceptibility to treatment [28].

According to the study by Brown et al. in the case of patients with PPROM treated prophylactically with oral erythromycin, they observed a change in the vaginal microbiota through the shift between Lactobacillus and Sneathia sanguinegens, through the abundance of the latter [19]. Thus, the administration of a probiotic would determine a decrease in this shift.

In the genus Sneathia of the vaginal ecosystem, a positive correlation was observed with genetic determinants responsible for antimicrobial resistance to macrolides (ermB) and tetracycline [tet(W)] [29]. The Sneathia sensitivity to antibiotics depends on the source from which the germs were collected. In the case of infection with Sneathia amnii, increased sensitivity to vancomycin was observed regarding the cultures from the vaginal microbiome compared to the resistance observed from the maternal blood [5].

CONCLUSION

Sneathia frequently defines the abnormal vaginal microbiome being involved in bacterial vaginosis. Although an underappreciation of Sneathia infection is observed, given the difficulty of establishing the diagnosis, establishing the role in the initiation and evolution of chorioamnionitis can lead to the prophylaxis and treatment of this infection in PPROM. A series of randomized studies will be needed to establish a series of precise recommendations regarding the efficacy and safety profile of some drugs. The association of a probiotic with antibiotic therapy improves the prognosis and decreases the recurrence rate of bacterial vaginosis in these patients.

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