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Normal and Premature Rupture of Fetal Membranes at Term Delivery Differ in Regional Chemotactic Activity and Related Chemokine/Cytokine Production

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Abstract

A gradient of immunological mediators exists in the fetal membranes from the periplacental zone (PZ) to the rupture zone (RZ) at term delivery (rupture of fetal membranes [ROM]). However, it is unknown if this gradient is different in premature rupture of these tissues (premature rupture of fetal membranes [PROM]). We therefore analyzed leukocyte chemotactic activity and chemokine/cytokine production in fetal membrane zones in ROM and PROM. In ROM, leukocyte chemotactic activity increased from the PZ to the RZ; however, this did not occur in PROM. This was due to consistently elevated leukocyte chemotactic activity in PROM compared to ROM tissues. In the RZ, ROM was characterized by increased T-cell attraction and high levels of chemokine (C-X-C motif) ligand 8 (CXCL-8)/interleukin 8, and PROM by increased granulocyte attraction and high levels of granulocyte-macrophage colony-stimulating factor and CXCL-10/interferon gamma-induced protein 10. We conclude that normal and premature rupture of fetal membranes differ in regional chemotactic activity and related chemokine/cytokine production, which may represent evidence for differential mechanisms of rupture at term delivery.

Keywords

chemotactic activity, fetal membranes, labor, leukocytes, PROM, ROM

Introduction

Normal labor begins at term in the presence of intact fetal membranes.[1] If there is no intervention, the fetal membranes remain intact until their spontaneous rupture near the end of the first stage of labor; this is termed spontaneous rupture of fetal membranes (ROM). The physiological mechanisms that normally lead to ROM prior to birth have been documented; however, the sequence of events that start and trigger ROM is currently unknown. Convention suggests ROM is precipitated by the stress of uterine contractions during labor; however, this fails to explain the 10% of term deliveries and 40% of preterm deliveries in which rupture is the initial clinically discernable event preceding any uterine contractions; this is termed premature rupture of fetal membranes (PROM).[2,3] Premature rupture of fetal membranes is a clinical complication which occurs before 37 weeks of gestation (preterm PROM) and is responsible for preterm births. Preterm birth currently accounts for most cases of neonatal morbidity and mortality.[4–6] To decrease preterm birth incidence, we have to understand the signal transduction pathways that are activated in PROM, as well as normal ROM.

Several studies have indicated that the fetal membranes undergo a genetically programmed, biochemically mediated, maturation process near term which is characterized by collagen remodeling and apoptosis.[7-11] Certain changes are limited to the region of the fetal membranes overlying the cervix referred to as the rupture zone (RZ).[12,13] It has been demonstrated that the RZ is a physically weak area overlying the cervical opening of the uterus that is characterized by expression of specific markers, suggesting that these regional characteristics develop prior to the onset of the contractions of labor

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and persist until delivery, when the rupture process occurs in this zone.[11,14,15]