Relationship of amniotic-type placenta inflammation to pPROM, PROM and risk of early onset neonatal sepsis

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Abstract

BACKGROUND: PROM and pPROM and early onset neonatal sepsis negatively affect the neonatal perinatal mortality and morbidity.
OBJECTIVES: The target of the work was to evaluate the relationship between chorioamnionitis, funisitis and PROM, pPROM and the risk of early onset neonatal sepsis.
METHODS: We examined 152 samples of the placenta and umbilical cord, histologically and microbiologically, in 53 women without PROM, 52 women with PROM and 47 women with pPROM.
RESULTS: We demonstrated a statistically significant relationship of chorioamnionitis and funisitis to the risk of early-onset neonatal sepsis. We demonstrated no relationship between pathological findings in the placenta and PROM or pPROM.
CONCLUSIONS: The histological findings of an amniotic-type placentitis can particularly be used for supporting or possibly excluding the diagnosis of early onset neonatal sepsis.

ORIGINAL ARTICLE

INTRODUCTION

The relationship between histological findings of the amniotic-type of placentitis, pPROM and early neonatal sepsis has been repeatedly published. These pathologic conditions actually negatively affect the development of the neonatal morbidity and mortality. A number of examinations, markers are being used to timely reveal consequences of these conditions. One of these examinations is the histological diagnostics of amniotic placentitis.

The target of the present communication is to verify the relationship between the histological findings of an amniotic-type placentitis and fu-

nisitis to pPROM, PROM and particularly to the risk of early onset neonatal sepsis Romero *et al* (1988), Unzeitig *et al* (l997), Romero *et al* (1998), Gomez *et al* (1997), Goldman *et al* (2008).

METHODS

The authors submitted 152 placenta and umbilical cord samples for microscopic examination. There were three groups of delivering women (53 women without PROM, 52 women with PROM after the 37th week of gestation and 47 women with pPROM before the 37th week of gestation).

In all the women, a smear for the bacteriological examination of the vagina and cervix was taken, and in newborns, the venous umbilical blood was sampled for the determination of levels of cytokines and sICAM-1.

Based on the examination of levels of cytokines and sICAM-1, the authors defined a group of 12 newborns with a risk of early neonatal sepsis onset Velemínský *et al* (2008).

Immediately after the delivery, we performed a thorough macroscopic inspection of the placenta focused on diffuse or spot like opacity of the chorion plate and possibly of the amnion and umbilical cord. On the umbilical cord, there can be nodes, which are recognised by the obstetrician. In the clinically suspect ascendant infection of the amnion, smears were also taken before the macroscopic inspection from the bottom area of the chorion plate for bacteriological examination. For the cultivation examination of the tissue, we took a long band of the amnion parallel with the placenta margin, at the vicinity of the placenta. The second long band of the amnion is taken parallelly with the opening in membranes formed during the delivery of the child. The bands of the amnion are coiled with the help of pincers and stored. The umbilical cord was examined on orthogradually taken transverse cuts of a segment close to the placenta and segment close to the child. At least two further sampling sites concern the chorion plate.

The histological examination of the placenta is preceded by a macroscopic description. It includes the placenta diameter, placenta height and umbilical cord anchorage. We also evaluated the shape of the placenta.

The central anchorage of the umbilical cord occurs frequently. Deviations of the umbilical cord anchorage are frequent but only those which cause a restriction of the blood inlet to the foetus in the course of the pregnancy or delivery, are of importance. Haematomas and thrombi can be present on the placenta and umbilical cord. The umbilical cord length (50–60 cm) and thickness (1.2–1.5 cm) are measured. Under normal conditions, two arteries and one vein are extended through the umbilical cord. In unique cases, in the umbilical cord, there is only one artery, which considerably affects the appropriate development of the foetus.

After the external examination of the placenta, tissue blocks were removed for histological examination. In the physiological course of the pregnancy, about 5 tissue blocks are sufficient for the preparation of histological mounts. Two blocks containing the chorion, a block containing the amnion and a block at the anchorage of the umbilical cord and in the terminal part of the umbilical cord were taken. In histological examination, in the chorion, there are commonly 'white infarctions', which are small necroses of villi and thrombi in adjacent sinuses. Small and infrequent infarctions are common in the placenta at the end of pregnancy. They exert no effects on the function. If these infarctions are large, as large as several cm, they can restrict the placental function and endanger the foetus. Large white infarctions are frequently present in the pregnancies with preeclampsia.

A macroscopic description of the placenta preceded histologic examination, including the placental diameter, placental height, and the site of umbilical insertion.

In the case of a known risk or pathologic course in the gestation, we obtained additional tissue blocks and, in the case of pathology on the histologic examination, the placenta was histologically-examined in a series of additional tissue blocks.

In the examination of the placenta for purposes of the present study, we specifically considered the histologic diagnosis of placentitis. The inflammation involved the chorion (chorionitis), amnion (amnionitis), or both (chorioamnionitis). The inflammation could extend to the funis (funisitis) and the recognition of inflammation of the funis is of a great importance for the diagnosis of the intra-amniotic infection (Keenan *et al* 1977).

The nature of the inflammation of the chorionic villi can be morphologically determined to a certain extent (Vogel 1996; Motlík and Živný 2001; Jungueira *et al* 1999).

In the differential diagnosis, it is necessary to take into account granulocytic infiltrates of non-infectious etiology in foetal acidosis after the removal of meconium due to pre-stasis and stasis in the subchorionic space as a consequence of a circulation disorder in the vessels of the funis. These infiltrates, in contrast to inflammatory reactions conditioned by the infection, exert no amniotropism. These infiltrates typically concern only one region, for example the subchorion fibrin layer or the circular infiltrate about the vein of the funis; amnionitis is not present.

The histologic examination of the placenta was performed as detailed by Vogel (1996). Placental histopathology in an extremely low weight infant was preformed by Verma *et al* (2008).

RESULTS

Table 1. Finding of chorioamnionitis in 152 delivering women

Group	Number of findings
A	11
B	10
C	10

Table 2. Finding of chorioamnionitis at risk for early neonatal sepsis (12)

	Chorio amnionitis	No Chorio amnionitis	Total
Risk group	10	2	12
Group without risk	21	119	140
Total	31	121	152

The difference between the finding of chorioamnionitis cases (31), i.e., group 2, and chorioamnionitis cases in the risk group (12), i.e., group 3, was significant at a $p<0.001$ (Fisher exact test).

Table 3. Finding of funisistis at risk for early neonatal sepsis (12)

	Funisitis	NO Funisitis	Total
Risk group	5	7	12
Group without risk	1	139	140
Total	6	146	152

Fisher exact test $p< 0.0001$.

Table 4. The most frequent microbiological finding in 10 cases of chorioamnionitis associated with a risk of early onset neonatal sepsis

Strains	Findings
MOP III	46.0%
MOP VI	27.0%
Streptococcus viridans	26.0%
Mycoplasma hominis	25.0%
Chlamydia trachomatis	23.0%
Escherichia coli	21.0%
Candida albicans	15.0%

In our group, there was no statistically significant relationship between a bacterial strain and the histologic finding of chorioamnionitis.

DISCUSSION

As a premature rupture of the membranes (PROM) we consider a condition, in which the spontaneous discharge of the amniotic fluid occurs still before the beginning of the delivery, i.e. in the absence of uterus contractions. This term is used by certain authors for the premature rupture of the membranes after the end of 37th week of gestation. If the amniotic fluid is discharged before the 37th week of gestation, then this condition is referred to as pPROM. The incidence of PROM reported in the literature is between 4 and 14% of gestation. In pPROM, i.e., premature discharge of amniotic fluid before the 37th week of gestation, an incidence between 2 and 3% has been reported (Gomez *et al,* 1997; Vogel, 2006; Unzeitig *et al,* 1997; Veleminsky *et al,* 2005).

Differences in data are specifically caused by different methods used for the determination of the diagnosis of PROM, demographic characteristics of the population investigated, or the type of studies.

The importance of PROM in the pathogenesis of the intra-amniotic infections is well-known (Romeo 1988, 1989, 1992, 1994, 1997, 2002), (Unzeitig *et al* 1997). There are also repeated references concerning the negative effects of intra-amniotic foetal infection on foetal mortality and morbidity of foetuses and newborns. Given the fact that we examined the microbial flora and not viral etiologies, we assumed the occurrence of the amniotic type placentitis. This assumption was found to be realistic.

The term amniotic type placentitis includes changes in the placenta itself, in amniotic membranes, and/or in the funis. There are many synonyms of this condition in the literature: *Amnionic sac infection syndrome*, *chorioamnionitis*, *intra-amniotic infection, or ascending infection* (in Vogel 1996). The process does not always involve all parts of the foetal cavity wall (*amniotic cavity)* uniformly; additional terms are also used: *Amnionitis* – inflammation in the stroma of the free amniotic membrane (synonym: *membranitis*). *Chorionic placentitis* – inflammation of the chorionic plate binding tissue (synonym *chorionitis*). *Vasculitis of the chorionic plate* – inflammation of branches of the allantoid vessels (synonym: *foetal plate vasculitis*). *Omphalovasculitis* – inflammation of umbilical vessels, where the vein is typically involved earlier and more than the artery (*umbilical cord vasculitis*). *Funiculitis* or *funisitis* – inflammation of Wharton's jelly (Vogel *et al,* 1996; Melis *et al*, 2007).

The histologic finding in the placenta corresponding to the amniotic type can be developed due to the infection, but also due to other causes (Goldman *et al* 2008). Some changes are described in the sense of hypoxic changes. The quality of findings is also associated with the age of the pregnant women (Long 2008). They are associated with necrosis of cells and tissues and exudation and proliferation of the binding tissues.

The necrosis and proliferation are equivalent to the inflammation prevalent, particularly in the embryonic and early foetal period, whereas the inflammation with cellular exudates is detected in the second and third trimesters. This is acute granulocytic and partially necrotizing inflammation of the amniotic membranes, chorionic plate, and/or umbilical cord. It is necessary to delimit a rare form of the course with the accumulation of macrophages and lymphocytes and multiplication of binding tissue cells in the amniotic membrane stroma. The inflammation can involve different parts of the amniotic cavity wall, i.e., the amnion, chorionic plate, or umbilical cord.

The term placentitis includes changes in the placenta itself, in the membranes or in the umbilical cord as a consequence of the infection or action of chemical agents. It can occur at any time during the course of pregnancy. Possible reactions depend on the age of the pregnancy.

In the differential diagnosis, it is necessary to take into account granulocytic infiltrates of non-infectious etiology in foetal acidosis after the removal of meconium due to pre-stasis and stasis in the subchorionic space as a consequence of a circulation disorder in the vessels of the funis. These infiltrates, in contrast to inflammatory reactions conditioned by the infection, exert no amniotropism. These infiltrates typically concern only one region, for example the subchorion fibrin layer or the circular infiltrate about the vein of the funis. The histologic examination of the placenta was performed as detailed by Vogel (1996), Vogel *et al* (2005).

In our sample, we demonstrated 20% of amniotic-type placentitis cases. There was a statistically significant finding of placentitis in the group at a risk of "early onset neonatal sepsis". Given the fact that microbiological examinations were not focused on virological examinations, we evaluate only the amniotic type of the inflammation.

CONCLUSION

By the examination of 152 samples of the placenta and umbilical cord, we established the diagnosis of amniotic-type placentitis in 20% and funisitis in 4.8% of women.

The results demonstrating the relationship to PROM and pPROM are statistically not significant.

In the relationship to the risk of early onset neonatal sepsis, we demonstrated a statistically significant association in cases of chorioamnionitis as well as funisitis.

We demonstrated no statistically significant relationship between the occurrence of a certain bacterial strain and finding of chorioamnionitis and funisitis.

Based on the results presented, the finding of the amniotic-type placentitis can be employed for the diagnosis of early onset neonatal sepsis to a limited extent only: with respect to a certain time interval between sampling the placenta and its histological examination. Thus, the histological examination can only help supplement the diagnosis.

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