

Editorial Focus

Amniotic fluid embolism: The complication of known pathomechanism but without pathogenetic therapy?

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The role of amniotic fluid cells in the initiation of intravascular coagulation in amniotic fluid embolism is the topic of the article by Zhou et al. (1) in the current issue of *Thrombosis and Haemostasis*. This is new information which can be considered as an argument for the basic mechanism of amniotic embolism related to disseminated intravascular coagulation/consumption coagulopathy (DIC). This research not only calls for comment itself but also provokes more general remarks on amniotic fluid embolism.

Amniotic fluid embolism is among the most dangerous complications of pregnancy, resulting in cardiopulmonary collapse and periparturient haemorrhage. It is the cause of some 10% of maternal deaths, and it occurs most often during vaginal delivery (70%) or immediately after it (11%), or during caesarean section or soon after it (19%) (2). In as high as 60–80% of cases amniotic fluid embolism results in the death of the mother and baby and, in cases of survival, serious and far-reaching complications have been observed, particularly in children.

Pathomechanism and new findings

Two components of native amniotic fluid, amniotic cells and tissue factor (TF) which used to be called tissue thromboplastin, are considered to be the main factors of the complication, whereas endothelin 1 and other amniotic substances seem only to be considered as supplementary factors. According to the earliest reports, cardiorespiratory collapse was supposed to be a consequence of the lung circulation blockage by amniotic cells or by amorphous elements. The belief that disseminated intravascular coagulation (DIC) is the main pathway of complication was emerging rather slowly – particularly after TF was identified in amniotic fluid, microemboli were found in pulmonary vessels, and especially after symptoms of DIC were perfectly documented (3).

On the surface of amnion cells, Zhou et al. (1) identified the phospholipid phosphatidylserine which is known to be externalised during cellular apoptosis. On the cell surface they also identified TF originating most probably from the soluble fraction of amniotic fluid. The authors assume that due to its negative

charge, phosphatidylserine can concentrate calcium-binding coagulation factors on the cell membrane and facilitate induction of intrinsic and extrinsic tenase activity followed by thrombin formation.

These results should be commented on: (a) They reconcile in a way two seemingly competitive views on the pathomechanism of amniotic fluid embolism, that is, the views about the mechanical blockage of pulmonary circulation by amniotic cells, and blockage caused by microemboli which are formed under the influence of amniotic TF; (b) The model by Zhou et al. of initiation and propagation of coagulation on the amniotic cells is a kind of obstetric equivalent of a cell-based model of haemostasis reported by Hoffman and Monroe III in 2001 (4).

Typical and atypical forms of amniotic fluid embolism

A new clinical option has been formulated – amniotic fluid embolism is diagnosed not only on the basis of pathomorphological analysis but also on the basis of the clinical image. Two clinical forms of this complication are currently recognised: (i) the typical form which is known from the first report by Steiner and Lushbaugh in 1941 (5), and (ii) the atypical form the description of which can be found in numerous case studies.

Symptoms of the typical clinical form have a phasic sequence: Cardiorespiratory collapse occurs first (phase 1), followed by consumption coagulopathy symptoms (phase 2), and dysfunction of kidneys (anuria) and other organs (phase 3), followed by distant complications. In contrast to typical embolism, cardiopulmonary collapse does not occur in atypical embolism but the first symptom is life threatening haemorrhage due to DIC. In one review on amniotic fluid embolism, 12% of patients have been found to have abnormal bleeding as the first symptom (6). Atypical embolism was observed, among others, during caesarean section or immediately after it, in cases of profound rupture of uterine cervix, as well as in the course of placenta abruption and in association with induced midtrimester abortion.

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Administration of heparin in amniotic fluid embolism

Can heparin have a positive influence on the efficiency of rescue procedures in amniotic fluid embolism? The question is not new but there seem to be reasons to ask it again. These reasons are: (a) On the one hand, the role of DIC in the mechanism of amniotic fluid embolism is accepted, and on the other hand, in new rescue procedures there is no mention of indications or contraindications for heparin application (7, 8) which implies resignation from this medication. (b) In my opinion, the first attempts to apply heparin in amniotic fluid embolism were burdened with methodological flaws, and therefore the negative opinion must be assumed to be uncertain. First of all, no procedural standards were recommended then, this partly being due to the chaotic nature of the procedure. Different doses were applied, the ‘dose-ef-

fect’ relation and the necessity of basic dose (bolus) repetition were not taken into consideration, and there was no adequate laboratory analysis before treatment or after every basic dose to estimate the heparinisation level. Furthermore, most controversial is the fact that heparin was applied in various phases of embolism, while the real need for heparin administration is limited to the beginning of this complication: surely, heparin is contraindicated in cardioarrest when the blood seems to be afibrinogenic, and during peripartur haemorrhage. Several years ago I promoted an active treatment program for the primary phase of amniotic fluid embolism using heparin (9), but this seems to have passed by unnoticed. I believe there is still a need for clinicians to reconsider and update their treatment program in regard to amniotic fluid embolism, something which could result in new observations on heparin application; discussion alone is not enough.

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