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Amniotic fluid embolism: 10-year retrospective study in a level III maternity hospital

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ABSTRACT

Objective: To provide updated data on amniotic fluid embolism (AFE) based on our population over a 10 year period, and to propose steps for improving current practice.
Study design: Retrospective study carried out in the Department of Gynaecology and Obstetrics at the Strasbourg University Teaching Hospital between 1 January 2000 and 31 December 2010. Dossiers of patients with AFE were identified using medical information system programme (MISP) coding and crosschecked with the pathology reports (hysterectomy, post-mortem examination).
Results: Eleven dossiers were found (0.28/1000). Eight cases (73%) of AFE occurred during labour, two (18%) in the post-partum period and one (9%) outside of parturition. Induction was initiated in four patients (45%) and labour sustained with oxytocin in 9 patients (90%). Acute circulatory collapse with cardio-respiratory arrest (CRA) was the herald symptom of AFE in 2 patients, and secondary cardio-respiratory arrest occurred rapidly in 6 patients (55%) following a relatively non-indicative prodromal phase. Disseminated intravascular coagulopathy (DIC) was observed in 10 cases (91%) and massive transfusion was necessary in all patients. Seven haemostatic hysterectomies (63%) were performed, with secondary arterial embolisation in 2 cases (22%). Although all patients presented a clinical picture of AFE, confirmation through histology or laboratory test results was forthcoming in only 7 cases (63%). Three patients died (27%). When AFE occurred during labour, 8 fetuses (75%) received intensive care support. In all, 11 newborns survived (85%). Their pH was less than 7.00 in 3 cases (27%) and 4 fetuses (36%) had an Apgar score of less than 5 at 5 minutes of life.
Conclusion: AFE is a rare but extremely serious disease. Some risk factors for AFE have been identified but they do not allow its occurrence to be predicted. The diagnosis may be supported by specific laboratory test results but only a post-mortem examination provides a pathognomonic diagnosis: unfortunately it is always retrospective. Obstetrical and intensive care management is complex and must be adapted to the situation bearing in mind the significant risk of haemorrhage and DIC. Hysterectomy must be performed if there is the least doubt.

1. Introduction

The definition and pathophysiology of amniotic fluid embolism (AFE) are open to discussion. For most clinical teams its definitive diagnosis is one of exclusion, and histological confirmation may be forthcoming only on post-mortem examination. Pathophysiologically, AFE may be the outcome of an accidental breach (rupture of the membranes and/or uterine veins, especially in the region of the cervix or isthmus) and a biological conflict [1]. There are several registers, some historical [2–5], which report regional or national figures on the incidence of this condition, and they may sometimes be at odds with each other. Abenhaim and Kramer [3,4] report similar incidences of respectively 6 and 7.7 per 100,000 births while Roberts [2] reports a lower rate (3.3/100,000 births). Although rare, AFE is the second cause of maternal mortality in France, accounting for 12% of deaths [6]. Similar proportions have been found in United States by Clark (10%) [5], and in Switzerland by Fässler (10%) [7]. The introduction of new recommendations and treatments for the management of major bleeding disorders, which are invariably present in AFE, has helped to improve its maternal and fetal prognoses, which nevertheless remain bleak. AFE is a disorder in which the rapidity and scale of the emergency

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response have a strongly determinant effect on the prognosis: it demands perfect coordination between the members of the various medical teams in order to ensure the patient is taken care of immediately.

The objective of this study is to provide updated data on AFE based on our population over a 10 year period, and to propose steps for improving current practice.

2. Material and methods

We conducted a retrospective study in descriptive epidemiology within the gynaecology and obstetrics hub in Strasbourg, which consists of a level 3 and a level 1 maternity unit, between 1 January 2000 and 31 December 2010. We decided to retain a strictly clinical definition of AFE based on the criteria listed by André Benbassa and Dominique Chassard in the national expert committee on mortality report published by the French Institute for Public Health Surveillance (InVS) [6], which matches that defined by Clark in 1995 [5]. A high suspicion of amniotic fluid embolism is defined as any situation in which the following are found in association:

- circulatory collapse (blood pressure $< 90/60$ mmHg) and/or cardio-respiratory arrest,
- acute hypoxia (O_2 saturation $< 90\%$),
- neurological signs (agitation, loss of consciousness, convulsions, coma)
- haemorrhagic syndrome associated with disseminated intravascular coagulopathy (DIC)-type coagulation disorders occurring in the peri- or post-partum periods.

Since the absence of lab test results or histological findings was not considered as an exclusion criterion, our dossiers were selected solely on the basis of clinical evidence. Dossiers were identified using cross-referenced searches of

- the standardised medical information system programme coding (known as PMSI in France and based on the ICD 10 classification) from the different gynaecology departments in the hub and from surgical intensive care,
- histology and pathology reports for all cases of haemostatic hysterectomy and post-mortems.

Maternal and obstetrical data analysed were age, parity, gestational age at the time of occurrence, ethnic origin, pregnancy type, possible triggering factors, condition of the membranes, abnormal fetal heart rhythm recordings, delivery method, maternal morbidity and mortality data, laboratory test results (squamous cells, Kleihauer test, serum tryptase), histological investigations in the event of hysterectomy or post-mortem reports in the event of death. The cyto-histological diagnosis of amniotic fluid embolism was based on the presence of intravenous amniotic material, especially fetal squamous cells. Fetal data analysed were weight at birth, gender, Apgar scores at 1 and 5 min after birth, pH at birth, and fetal morbidity and mortality.

Perinatal clinical data were complemented with histological findings (post-mortem report, histological analysis of the hysterectomy specimen) and screening tests for cytological and laboratory parameters: screening for squamous cells in peripheral maternal blood and in broncho-alveolar secretions as well as assay of maternal serum tryptase.

Comparisons between the AFE group and the general population were carried out using Chi-square test for categorical variables and Student's t-test for continuous variables. A p-value <0.05 was considered as statistically significant. The statistical software package SAS version 9.3 (SAS Institute Inc., Cary, NC, USA) was used for data analyses.

3. Results

A total of 38,717 births were recorded between 1 January 2000 and 31 December 2010. Of the 14 dossiers found on the basis of our research methodology, 11 met the above-listed inclusion criteria. Three dossiers were not included because the available clinical data were insufficient to allow us to conclude that there was a high index of suspicion of amniotic fluid embolism.

The incidence of amniotic fluid embolism was 28/100,000 births and occurred in 10 singleton pregnancies and one triplet pregnancy. The median maternal age was 32.6 [24–43], the median parity was 1.27 [0–3], median gestational age 40 weeks [31^{+6}–41^{+5}]. During this same period in our general population in the maternity hub at the Strasbourg University Teaching Hospital, the median maternal age was 29.3 ($p = 0.05$), for a median parity of 0.94 (not significant). Of the 11 patients, 5 (45%) were migrants. Concerning the obstetrical context, 8 cases of AFE (73%) occurred in the peripartum period, 2 (18%) occurred immediately postpartum ($<$2 h) and one (9%) during a scheduled caesarean section. Six patients (55%) had labour induced with misoprostol (3/6), dinoprostone (2/6) or oxytocin (1/6). In the general population, the rate of induced labour was 20.1% ($p < 0.0001$), with 21.0% ($p < 0.0001$) caesarean sections. When AFE occurred, the membranes had ruptured in all cases, either spontaneously (45%) or artificially (55%). Oxytocin was used to augment labour in 9 patients (90%). Uterine hypertonia was noted in 4 patients (40%).

Maternal herald signs were respiratory (dyspnoea, oxygen desaturation), cardiovascular (syncope, malaise, collapse, cardio-respiratory arrest (CRA)) and/or haemorrhagic. It should be noted that in the six cases in which CRA occurred it was the inaugural event twice (33%). In every case, the clinical picture progressed towards that of a sustained post-partum haemorrhage and worsened in 91% of cases due to DIC.

Impairments of fetal heart rhythm were invariably found in parallel with the maternal symptoms. Obstetrical care was provided to 8 fetuses (those *in utero* at the critical moment). Extraction was in all cases performed within 20 min, and in 5 cases (62.5%) within 5 min of the initial symptoms, with 7 emergency caesarean sections and one vacuum-assisted extraction. All patients developed post-partum haemorrhage, and surgical intervention to achieve haemostasis was necessary in 7 of them (64%). On two occasions the team had to ligate the uterine and hypogastric arteries, followed by haemostatic hysterectomy. Five haemostatic hysterectomies were performed immediately, and two of these patients required additional embolisation by means of interventional radiology. In total, all 7 patients who presented a post-partum haemorrhage refractory to medical treatment underwent a hysterectomy.

Resuscitation care was always needed. Of the 6 patients with CRA, external cardiac massage was sufficient in one case, but 5 (83%) required application of external electric shock. Extracorporeal membrane oxygenation (ECMO) with veno-venous cannulation was necessary in two cases. Transfusion of labile blood products was always necessary with a median transfusion of 11 units of packed red cells, 11 units of fresh frozen plasma and 2 units of activated platelets. Fibrinogen infusions (Clottagen®) were used in 6 patients (55%) and factor VIIa (Novoseven®) in 2 patients (18%).

All patients who presented with AFE were admitted to the intensive care unit as a consequence of this severe maternal condition. In terms of co-morbidity, a single case of amnesic syndrome and a single case of complete thrombosis of both ovarian veins were observed, the latter resolving satisfactorily after a curative dose of antithrombotic. Of the 11 patients, 3 died (27%). Maternal mortality as a consequence of AFE was therefore 7.8 per 100,000 births. During the same period, 6 other maternal deaths