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Maternal pulmonary embolism due to amniotic fluid : review of the literature

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MATERNAL PULMONARY EMBOLISM DUE TO AMNIOTIC FLUID

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MATERNAL PULMONARY EMBOLISM

DUE TO AMNIOTIC FLUID

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MATERNAL PULMONARY EMBOLISM DUE TO AMNIOTIC FLUID

Review of the Literature

In 1941, Steiner and Lusbaugh (13) first described pulmonary embolism due to amniotic fluid as a disease entity. At that time these investigators reported eight cases in which this condition was present and in which they believed it to be the immediate cause of death. Since that time, a total of eighteen cases of maternal death have been reported in which this condition was believed to be the immediate cause of death or a contributory cause of death.

The condition is manifested clinically by a sudden onset of shock with dyspnea, cyanosis and death within a short time.

Microscopic examination of lungs of these patients reveals emboli composed of epithelial squamae, meconium and lanugo hairs lodged in the pulmonary arteries, arterioles and capillaries. Animal experiments were made to establish the relationship between the embolization and the clinical observations. Conclusions drawn from these experiments were that embolization of the pulmonary vessels with amniotic fluid can cause shock and death.

The discovery of this condition as a disease entity has made it possible to diagnose some cases of maternal death which pre-

viously were misdiagnosed or inadequately diagnosed among which are:

1. Some cases of unexplained obstetric shock.
2. Certain cases of postpartum uterine atony with hemorrhage.
3. Idiopathic hemoptysis of pregnancy.
4. Non-convulsive toxemias.
5. Acute pulmonary edema of pregnancy.

Clinical Picture

The clinical picture of pulmonary embolism due to amniotic fluid is characterized by the sudden onset of (1) a sensation of chilliness, (2) restiveness, (3) precipitous drop in blood pressure, (4) fear of impending death, (5) tachycardia, (6) cough, (7) dyspnea, and (8) cyanosis. This may occur before onset of active labor, during labor or soon after delivery, most frequently near the completion of the second stage.

All proved cases have terminated in death within a relatively short period of time, averaging eight hours and 36 minutes. Only one patient survived longer than eight hours and only seven patients (26.9%) survived longer than two hours. The longest survival was seven days and the shortest was described as immediate death.

Seltzer and Schuman (11) have reported a case of profound shock in a parturent female which they believed to be due to pulmonary embolism by amniotic fluid. Since this patient recovered, however, the diagnosis could not be proved.

The authors ascribe the recovery of this patient to the following factors:

1. She was a young woman in good condition and was not tired by a long labor.

2. She was under a general anesthetic at the time of embolization.

3. The condition was suspected early and treated accordingly.

4. The apparent rapid rate of removal of the particulate matter from the lung fields as shown by radiography.

These authors consider the adequate treatment to consist of the "interdiction of intravenous fluids or the very slow administration of whole blood in the presence of pulmonary edema, atropinization, morphine and oxygen." (11)

Pathological Findings

The gross pathological findings in cases of pulmonary embolism due to amniotic fluid have been for the most part limited to occasional pulmonary edema, (34.6% of cases). One report (15) listed a tear in the placental membranes with extension of amniotic fluid into the broad ligaments. Two cases were reported as having ruptured uteri. (8 and 13) Abruptio placenta was a gross finding in a case reported by Steiner and Lushbaugh, (13) and placenta previa was reported in two cases. (10 and 13)

On examination of uteri in these cases, surgical incisions or tears into myometrium or endocervix, which could have been the point of entry of amniotic fluid into the maternal circulation, are noted in about fifty per cent of patients.

In no case was the diagnosis of pulmonary embolism due to amniotic fluid made on gross examination.

Microscopically, the condition is characterized by embolization in varying degree of the pulmonary arteries, arterioles and capillaries by the contents of amniotic fluid. These emboli consist of the components of meconium, vernix caseosa and occasionally lanugo hairs.

Vernix caseosa is identified by an amorphous material which is believed to be the ground substance of the vernix and desquamated

squamous epithelium. The latter is found mixed with the amorphous material and is best demonstrated with Mallory's connective tissue stain which imparts coloration ranging from yellow to orange to red or purple and occasionally dark blue-black. (13) The amorphous sebaceous material is eosinophilic in varying degree in a manner very similar to neutral fat.

Meconium is composed of desquamated epithelial cells and mucin, the latter of which is found in small arteries for the most part. Mucin is readily identified as such with hematoxylin and eosin stain when it is present in fairly large collections or when it is not too heavily infiltrated with leukocytes (as it becomes within a relatively short time.) Occasionally, therefore, it is necessary to stain the material with specific mucin stains for positive identification. As do most of the elements of these emboli, mucin has a variable staining reaction. Usually it is basophilic and may be slightly eosinophilic, but, regardless of this, it will always take the specific stains.

Mixed with the mucin are found variable numbers of poorly stained objects resembling swollen, degenerating epithelial cells and occasionally leukocytes. (13)

Lanugo hairs have been demonstrated only rarely, specifically in only four of twenty-six cases (15.3%). (7), (8), (9) and (10)

Emboli with high mucin content tend to lodge in the small arteries, whereas those composed of squamae and amorphous material more readily pass into pulmonary arterioles and capillaries.

Embolized vessels almost always show an increase in leukocytes, the increase being proportional to the duration of the condition. There is a bloodless area around the squamae usually, but it has been pointed out that leukocytes around mucous tend to be in parallel rows, giving it a combed out appearance. (9)

Examination of the microscopic sections of a lung of the patient who survived seven days after onset of the actue episode, revealed small granulomas with foreign body giant cells surrounding the embolic material. The reaction to the pulmonary embolic materials was not as great in seven days as might be expected on the basis of the observations in dogs. In the dog experiments, however, the injected material was not kept sterile and, therefore, some of the reaction may have been on the basis of bacterial invasion. (8)

Embolization of arteries apart from the pulmonary circulation has been noted in three cases. Two had amniotic contents in renal and omental vessels, and one report noted that emboli were found in arteries of the brain, heart and in myocardium. (12 and 16)

The presence of amniotic fluid contents in the uterine sinusoids and pelvic veins was noted in a high percentage of cases in which its presence was sought.

In an autopsy of one of their patients, Gross and Benz [4] obtained blood from the inferior vena cava and the right side of the heart which they centrifuged and were able to identify squamae from amniotic fluid. They found the squamae in a fluffy layer above the usual leukocytic cream. As a result of these observations, these authors suggest that blood be aspirated from the right heart and examined in this manner to lend credence to the diagnosis of embolism due to amniotic fluid in those cases where the condition is suspected and permission for autopsy cannot be obtained.

Animal Studies

In the original investigation by Steiner and Lushbaugh, extensive animal studies were carried out to determine,

> "(a) whether amniotic fluid and also meconium could produce death when introduced into the vascular system, (b) whether the clinical picture in such animals could be similar to that seen in the women, (c) whether the changes in animals' lungs would resemble those seen in human lungs and finally, (d) whether the known material injected into the animals would have the same histologic staining

reactions and general structure as the unknown material discovered in human lungs." (13)

The experiments consisted of injecting diluted human meconium, human amniotic fluid and filtered human amniotic fluid into the ear veins of rabbits and the intravenous injection into dogs of mixtures of human amniotic fluid and meconium.

For the rabbit experiments, meconium was obtained from the sigmoid colon of a recently dead fetus and diluted with physiologic saline solution to about four times its original volume. Injection of this mixture caused "anaphylactoid" death in two rabbits at about ten and thirty-five minutes and autopsy disclosed the findings typical of human cases, e.g., emboli composed of mucin, epithelial squamae, leukocytes and amorphous material in small arteries, with all these materials except mucin in the arterioles and capillaries. A third rabbit which was given a smaller dose was killed after six hours and showed minimal embolization but rather marked pulmonary edema. The first two rabbits reacted to the injections by first becoming restless, then dyspneic followed by convulsions and death. The third animal showed only restlessness and refusal to eat.

Injection of undiluted human amniotic fluid into the ear veins of two rabbits showed comparable results with the exception that there was no mucin found in the pulmonary emboli.

Filtered human amniotic fluid injected into four rabbits intravenously produced no detectable pathology.

For the dog experiments, fresh human meconium taken from the intestines of dead newborn infants was diluted with fresh human amniotic fluid in the proportions of one Gm. meconium to four cc. of fluid. This mixture was injected intravenously in varying dosages into seven dogs while a one Gm. to nine cc. mixture was used on two dogs.

Atropine sulfate was given to five dogs (o.2 mgm./Kg) intravenously ten to fifteen minutes prior to the meconium-amniotic fluid mixtures in order to see if depressor reflexes from the emolized lungs could be minimized and thereby reduce the severity of the reactions.

All dogs, except one which received a small dose and had atropine, showed shock reactions which began in about thirty seconds and consisted of restlessness, dyspnea, nausea and vomiting, tachycardia, cyanosis and occasional diarrhea. Cardiac irregularities were noted in dogs with heavy dosages.

The severity of the reactions apparently was reduced by the injection of atropine though the shock reaction was not prevented or abolished thereby. It was noted that the severity of reaction varied directly with the dosage of embolizing material.

The conclusions gained from animal experiments are then that human meconium and amniotic fluid can produce death when injected into the vascular systems of rabbits and dogs. When embolism was heavy, these animals showed the clinical picture of anaphylactoid reactions. When death was not too sudden, pulmonary edema developed.

Microscopically and grossly, morphologically and by staining reactions, by location, the picture produced in animals paralleled those seen in human beings. It was found that the degree of leukocytic infiltration paralleled the length of survival. This may have been due to bacterial invasion of the injected material prior to its use, however, since precautions were not taken to keep the material sterile. (8)

The fate of these emboli appeared to be first their lodging in the pulmonary vascular bed followed by their rapid infiltration with leukocytes. They apparently do not pass into the general circulation except in rare instances.

In dogs, the emboli are gradually recannalized and are then partly or completely removed, presumably by phagocytosis. There were granulomatous lesions found at seven days but had been resolved at the end of fourteen days.

TABLE I

Case*	Age	Paraty	Gestation In Weeks	Labor	Onset of Shock	Shock	Cyanosis	Pulmonary Edema
(13) Case #1	30	2	38	Intermittent 48 hours then violent pains	At same time as violent pains 1¼ hours before normal delivery	+	+	
(13) Case #2	26	1	42	31 hours strong contractions	After 31 hours labor	+	+	+
(13) Case #3	28	4		Short and strong	Soon after delivery	+		+
(13) Case #4	37	3		Strong pains	Soon after delivery	+		+
(13) Case #5	42	8		Precipitate	Soon after delivery	+	+	
(13) Case #6	34	2	48	Severe	3 hours before delivery	+	+	+
(13) Case #7	33	4		Strong	Soon after delivery	+		
(13) Case #8	25	2		2 days inertia then strong labor	At same time as severe pains	+		+
(8) Case #1	35	2	40	4 hours low forceps	During labor	+		
(8) Case #2	38	4		Placenta previa lower segment section	Soon after delivery	+		

*Number in parenthesis refers to author as shown in bibliography.

TABLE I

Survival After Onset of Shock	Survival After Delivery	Amniotic Fluid Abnormalities	Size of Fetus in Grams	Condition of Fetus	Other Factors in Shock
3 hours 45 min.	2 hours 25 min.			Macerated	Post partum hemorrhage after 3rd stage. Uterus packed
1 hour	Died without delivery	Meconium	3345	Alive until death of mother	
8 hours	8 hours	Meconium	4054	Living	Moderate post partum hemorrhage
1½ hours	1½ hours	Meconium and old blood	4536	Dead	Abruptio placenta post partum hemorrhage after onset shock
50 min.	55 min.			Living	Mild controlled thyrotoxicosis and chronic endocarditis. Placenta previa
5 hours	2 hours	Meconium	5076	Dead about 8 hours	Post partum hemorrhage after onset of shock
2 hours	2 hours		5472	Living	Mild diabetes M.
2 hours	Died without delivering		3600	Dead for 2 weeks	Ruptured uterus
7 days	7 days			Dead	Ruptured uterus ** during first stage undiagnosed
3 hours	3 hours			Living	Toxemia - hem-** orrhage at operation

**Maternal pulmonary embolism due to amniotic fluid was not cause of death.

TABLE I - Continued

Case*	Age	Paraty	Gestation In Weeks	Labor	Onset of Shock	Shock	Cyanosis	Pulmonary Edema
(4) Case #1	25	2	43	13 hours, 45 min. first stage tetanoid contractions	At full dilatation	+	+	
(4) Case #2	42	3	39	Pituitrin given for inertia. Tetanic contractions 24 hours later. Forceps after 1 hour 2nd stage	At delivery	+	+	
(4) Case #3	35	5	36	8 hours 1st stage-15 min. 2nd stage-normal 3rd	20 min. after delivery	+		
(3) Case #1	40	6	42	Normal labor 3 hours duration	Two hours after delivery of dead infant	+	+	+
(5) Case #1	33	2	42	Inertia 36 hours then strong labor → delivery in 4½ hours	With severe pains	+		+
(15) Case #1	25	2	44	Normal 1st stage 3 hours	After full dilatation	+	+	
(16) Case #1	30	1		Normal labor 2 to 3 hours	When started to crown	+	+	
(7) Case #1	28	1	28	9 hours not unusual contractions	Just after membranes ruptured at 5 cm. dilatation	+	+	
(1) Case #1	32	3	40	Delivered by Caesarian section-no mention of labor	Seven min. after incision of uterus and 5 min. after delivery	+	+	

*Number in parenthesis refers to author as shown in bibliography.

TABLE I - Continued

Survival After Onset of Shock	Survival After Delivery	Amniotic Fluid Abnormalities	Size of Fetus in Grams	Condition of Fetus	Other Factors in Shock
40 min.	5 min.			Dead	
1 hour 15 min.	65 min.	Hydramnios		Dead	
1 hour	80 min.	Fresh blood		Living	
Not recorded but probably in 1 hour	± 3 hours post partum	Not noted		Dead	
4 hours 45 min.	45 min.	Blood	3400	Dead	
5 min.	Died Undelivered		3375	Dead	
15 min.	Died Undelivered	Little meconium	2735	Died when mother died	
10 min.	Died Undelivered	Bloody		Died after Caesarian section premature	Premature
7 hours	5 hours	Heavy meconium particles of bile stained vernix	4190	Died 5 min. after delivery	Placenta previa

TABLE I - Continued

Case*	Age	Paraty	Gestation In Weeks	Labor	Onset of Shock	Shock	Cyanosis	Pulmonary Edema
(1) Case #2	31	1		Not unusual labor pains about 8 hours	During laparotomy to stop uterine hemor.			
(14) Case #1	44	4	42	14 hours mild to moderately severe labor	While walking about after 14 hours labor	+	+	±
(12) Case #1	32	2	41½	Medical induction strong pain after 3rd dose of pituitrin	10 min. after onset-severe pains	+	+	+
(10) Case #1	23	1	43	Medical induction with ruptured membranes. Mild labor for 9 hours then strong contractions	When crowning	+	+	
(9) Case #1	38	2	40+	Inertia for 2 to 4 days then severe cramps	Awakened by severe pain after 2 to 4 days inertia	+	+	+
(9) Case #2	39	3		Mild labor then pituitrin → active labor	After about 1 hour active labor	+	+	
(9) Case #3	31	8	40	Strong precipitous delivery	3 hours after precipitous delivery			
(11) Case #1	18	1	45	Medical induction 1st stage 8½ hours	18 min. after breech delivery	+	+	+

*Number in parenthesis refers to author as shown in bibliography.

TABLE I - Continued

Survival After Onset of Shock	Survival After Delivery	Amniotic Fluid Abnormalities	Size of Fetus in Grams	Condition of Fetus	Other Factors in Shock
Immediate				Living	Small Amount uterine bleeding from 3 hours from onset of labor until del.-persis. p.p.h.
Within 15 min.	Died undelivered	Not noted	3320	Dead	
30 min.	Died undelivered	Hydramnios fresh blood	3825	Alive until death of mother	
Not recorded but about 30 min.	Died immediately following delivery	Not noted		Dead	Placenta previa
50 min.	Died undelivered	Bloody	4500	Dead	
3 hours	2½ hours			Dead	
35 min.	3 hours 35 min.	Blood tinged	4300	Living	
	Patient recovered	Undiluted meconium	2782	Living	Blood loss 150 cc.

Review of Case Reports

Review of the case reports shows that this condition occurs most frequently in multiparous females over the age of thirty-two years who are past term and whose babies are somewhat heavier than average.

The average age of patients in this group was 31.8 years with a range of twenty-three to forty-four years. Thirty-three per cent were below the age of thirty, whereas thirty-eight per cent were thirty-five or older.

The average paraty of patients in the group was three with a range of one to eight with the ratio about one para I to five plus multipara. (Schenken et al report that in a random survey of normal deliveries at Nebraska Methodist Hospital revealed a ratio of about one primipara to eight multipara). (10)

Forty-two and seven-tenths per cent of the total cases and 68.6% of the cases in which duration of the pregnancy was noted were past forty weeks' gestation.

In those case reports, which listed the weight of the fetus, 64.3% exceeded the average birth weight of 3400 Gm., (6) and 92.8% exceeded 3300 Gm., or $7\frac{1}{4}$ pounds. (See table I)

Many of the patients had strong, severe or tetanoid contractions for the most part after the membranes had ruptured spon-

taneously or surgically. These factors may indicate that amniotic fluid is forced into the uterine sinusoids by powerful contractions when the outlet is blocked by a large fetus. Often the fetus has been dead or in definite distress, which would tend to cause expulsion of meconium into the amniotic fluid. (2)

That strong labor pains are necessary to cause this condition, however, is definitely not true as is shown by the report of Case #2 of Lushbaugh and Steiner (8) and Case #1 of Barron, Sturley and Lindsay (1) in which the patients never went into labor. Other patients in this series had nothing more than "normal labor."

Incidence

The incidence of pulmonary embolism due to amniotic fluid was once believed to be about one in eight thousand normal births. (13) After study of more cases, however, it must be concluded that the occurrence is much less than that figure. The original estimation was made on the basis of three cases in 24,000 deliveries at the Chicago Lying-In Hospital. There have been no additional cases, however, in 26,000 deliveries since that time at the same hospital. (14)

Mechanism of Embolization

Although there are many factors which play a part, the most important single factor in causing amniotic fluid to enter

the maternal circulation is an abnormal opening in the uterine vessels, either decidual or myometrial. (17) These abnormal openings can be caused by uterine or cervical tears, placenta previa, premature separation, ruptured uterus or Caesarian section.

It would seem that the additional factors of strong labor contractions, the large fetus and the rupture of the membranes supply the necessary factors to produce an embolization of sufficient magnitude to produce the more profound reactions. The fact that the condition has occurred in the absence of labor, of course, is proof that none of these latter mechanisms is necessary for its production.

Since it has been shown both experimentally and clinically that the severity of the reaction is in part proportional to the degree of embolization and since there is wide variation in the reported cases in the conditions which are the apparent cause of the condition, the severity of the reaction evidently is a resultant of the following factors.

1. The total surface of exposed blood vessels.

2. The pressure, positive or negative, to which the amniotic fluid is subjected.

3. The duration of the period of embolization.

Summary and Conclusions

1. The literature on maternal pulmonary embolism due to amniotic fluid is reviewed, and the pertinent data from the recorded cases is presented in table form.

2. Maternal pulmonary embolism due to amniotic fluid is established as a cause of death or a contributory cause of death as shown by clinical and experimental evidence.

3. The condition is manifested clinically by the sudden onset of shock, usually without apparent reason, which is associated with chilliness, anxiety, cyanosis and dyspnea. It occurs most frequently in multiparous females past the age of thirty-two, whose babies are larger than average.

4. Pathologically the process is characterized by embolization of pulmonary arteries, arterioles and capillaries by the contents of amniotic fluid.

5. Emboli gain access to the maternal circulation through abnormal openings in the uterine veins, aided in varying degree by hard labor pains and/or the obstruction of the pelvic outlet by a larger than average fetus or the negative pressure of the utero-pelvic veins.

6. The severity of the clinical reaction varies directly with the magnitude of embolization, the premedication and the physiological state of the patient at the time of embolization.

7. The possibility of sublethal embolization by amniotic fluid is attested by experimental and clinical observations and supported by pathological studies.

8. The incidence of pulmonary embolism is difficult to establish due to the relatively small number of reported cases. A reasonable estimate would be about one in twenty-five to thirty thousand births.

9. In reviewing the literature on the subject of pulmonary embolism by amniotic fluid, one is impressed with the unfortunate lack of adequate descriptions of the clinical cases. More meaningful analyses of the condition and establishment of the pathogenesis could be made if these reports described more fully the type and duration of labor, the size of the fetus and its condition as the labor progresses, the estimated blood loss, the amount and character of the amniotic fluid, the placenta and an adequate estimation of the relative importance of any other factors which could be responsible for the onset of shock and death.

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