CLINIC OF VAGINAL FLOGOSIS DUE TO MYCOPLASMA DURING PREGNANCY

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SUMMARY

The AA. report the results obtained isolating both M. Hominis and U. Urealyticum in the vaginal exudate of 20 patients with premature membrane's rupture between the 32nd and 38th week of gestation and in that of 50 patients with complete membranes, who had delivered between the 38th and 42nd week of gestation.

No significative correlation has been found between the percentage of mycoplasma's isolation and a higher frequence of premature membrane's rupture.

The clinical importance of vaginal flogosis during pregnancy, is also demonstrated by the continuous and more and more frequent reports in literature of pathological conditions both foeto-maternal and neonatal due to alterations of the vaginal echosystem.

In addition to agents certainly pathogenous as Streptococcus β-haemolyticus, Haemophilus vaginalis, Candida albicans and Trichomonas vaginalis, which can interfere negatively on pregnancy, there are recent signals of possible negative repercussions due to mycoplasmas on the phisiologic course of pregnancy.

In 1955 Edward and Freundt used the term « mycoplasma», already proposed by Nowack in 1929, to classify taxonomically some microorganisms considered biologically intermedious between bacteria and viruses.

In 1898 Nocard and Roux (1) isolated for the first time from the lung of a bovine who died of pneumonia, a microorganism (Mycoplasma micoides), subsequently called PPLO: pleuropneumonia-like organism.

The aetiological role of mycoplasmas in a human disease was demonstrated in 1941 by Eaton et al.; till nowadays this certainty exists only in case of relations between mycoplasma pneumoniae and primary atypical pneumonia (PAP). Anyhow, « Eaton agent » was not the first described in human, because already in 1937, Dienes and Edsall (2) isolated a strain of mycoplasma from an abscess of a Bartholin's gland. The importance of Eaton's discover is due to the fact that mycoplasmas were for the first time considered as certain aetiological agents of a human pathological condition.

Since then, particularly in the male and female genitourinary apparatus, various strains of mycoplasmas were isolated, however without a definitive demonstration of their aetiological significance.

In 1954, Shepard isolated the so called T-strains (3), which are with the Mycoplasma hominis the most interesting for the obstetrician and gynaecologist.

Mycoplasmas, taxonomically distinct from the bacteria (Schizomycetes) and viruses (Microtatobiotes), are now included in the class of the Mollicutes made up by two different families, Micoplasmataceae and Acheloplasmataceae, and three genera, *Mycoplasma* (with more than 40 species of which 7 isolated in the human), *Acholeplasma* (5 species), and *T-strains Ureaplasma* (1 species) Mycoplasmas are the

smallest known organisms having an autonomous life (not citodipendent), characterized by an extreme pleomorphism due to the lack of a cellular wall. As the bacteria, they have no nuclear membrane, they present ribosomes and the capacity of developing on an acellular medium. They differ for the absence of mesosomes and citoplasmic inclusions, for the shape and dimensions which vary from the minimum filtrable reproductive unit (100-125 nm) to the spherical (500 nm) and long forms (5 um).

They have in common with the viruses the dimensions, being the minimum reproductive unit often smaller than the myxoviruses and paramyxoviruses, the partial filtrability and citopathogenicity; even the « neutralization », according to some Authors, is a common property of mycoplasmas and viruses. The reproduction of mycoplasmas is inhibited by antibodies in absence of complement.

Mycoplasmas generally form colonies of very reduced dimensions and observable only under the microscope. On the basis of the morphology of the colonies, they are divided into three categories: the first includes those classified as «large colonies», defined as «fried egg», characteristic of *Mycoplasma hominis*; the second the granular ones without a halo, characteristic of *Mycoplasma pneumoniae*; and finally the third, including the very small granular and dark ones characteristic of *Ureaplasma urealyticum*.

Still is not quite clear the part played by the mycoplasmas in giving rise to some human diseases. It must be pointed out that, only in case of PAP is certain the mycoplasmic aetiology, even if 21 human diseases are suspected to have a mycoplasmic aetiology [4].

Eventhough is not yet certain the real aetiologic role of mycoplasmas in relation with obstetric pathologic conditions [34], anyhow many Authors report cases of repeated abortion [5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15], of amnionitis [16, 17, 18, 19] with more or less severe perinatal and neonatal infections [15, 16, 20, 21, 22, 23], of post-partum fever and even sepsis [24, 25, 26, 27], of premature labours due to spontaneous membrane's rupture and « small for date » neonates [13, 29, 30].

In the cases just mentioned, Mycoplasma hominis and Ureaplasma urealyticum were isolated and subsequently identified in the vaginal fluor and in the biologic fluid examined.

The purpose of our trial is to verify if the isolation of Mycoplasma hominis and of Ureaplasma urealyticum at vaginal level, is correlated to a more frequent premature membrane's rupture and/or to « small for date » neonates.

MATERIAL AND METHODS

The investigation was conducted on patients admitted to the Obstetric and Gynaecological Clinic of Padua's University, divided into two groups.

The first group included 20 patients with premature membrane's rupture between the 32nd and 38th week of gestation who had delivered within three days from the hospitalization. The second group included 50 patients hospitalized to have their baby between the 38th and 42nd week of gestation.

The samples were obtained from the posterior vaginal fornix, after the introduction of a sterile vaginal speculum and visualization of the cervix, using two swabs respectively for the culture tests and to prepare the specimens for the microscopic examination.

The culture media used for mycoplasmas were those already described by different AA. [31, 32], but with some modifications [33].

The vaginal swabs were immediately put in test-tubes containing 1ml of « mycoplasma transport broth », BMB (70 % Triptic Soy broth, 20 % Horse serum not warmed up, 10 % of yeast extract, 0.002 % of red phenol and 500UI/ml of penicillin) and 50 μg/ml of B-Amphotericin; the pH was corrected with HCl 1N to 6.2 ± 0.1.

The vaginal exudates were put in a culture media within maximum two hours from the drawn, or they were preserved at — 25 °C for not more than 7 days.

The microbiological examination was carried out at the Microbiology Institute of Padua's University, according to techniques previously described [33].

RESULTS

In the group of 20 patients hospitalized for premature membrane's rupture, the percentage of mycoplasma's isolation from the vaginal exudate has resulted to be of 45% (tab. 1); in particular M. hominis has never been isolated alone, while in 10 % of the cases it was isolated with U. urealyticum.

Table 1. — *Percentage of mycoplasma's isolation and birth weight in the 20 cases of premature membrane's rupture.*

N. Cases	M. Hominis	U. Urealyticum	U. Urealyticum + M. Hominis	Birth weight	Week of gestation
1)		+		2620	36
2)		+		2650	34
3)				1820	32
4)				1670	32
5)		+		2840	36
6)				2700	35
7)			+	2400	36
8)				1760	33
9)		+		2360	35
10)		+		2490	35
11)				2860	35
12)				2480	33
13)		+		1640	32
14)				2700	34
15)			+	3430	36
16)				3100	36
17)				3580	38
18)		+		1840	33
19)				2780	36
20)				2200	34
	0 (2)	7 (2)	2		
	10 %	45 %	10 %		

Table I also reports the birth weights, at the different weeks of gestation, of the neonates of mothers having positive or negative mycoplasma's research. In figure I the birth weights are compared with the centiles, at the different weeks of gestation, obtained through an analysis carried out in our Clinic on 11.226 at term pregnancies ([36]).

The centiles at the different weeks of gestation, represent the mean of the weight's centiles in the two sexes.

In the group of 50 patients with complete membranes, hospitalized to delivery, the percentage of mycoplasma's isolation from the vaginal exudate, has resulted to be of 52 % (tab. 2); in particular M. Hominis has never been isolated alone, while

Table 2. — *Percentage of mycoplasma's isolation and mean (± SE) of birth weights in the 50 cases of at term pregnancies.*

	N. Cases	%	Mean birth weight ± SE
Negative	22	44	3130 ± 250
Positive M. Hominis	0 (9)	(18)	3140 ± 380
Positive U. Urealyticum	17 (9)	(52)	3280 ± 320
Positive M. H. + U. U.	9	18	3060 ± 210

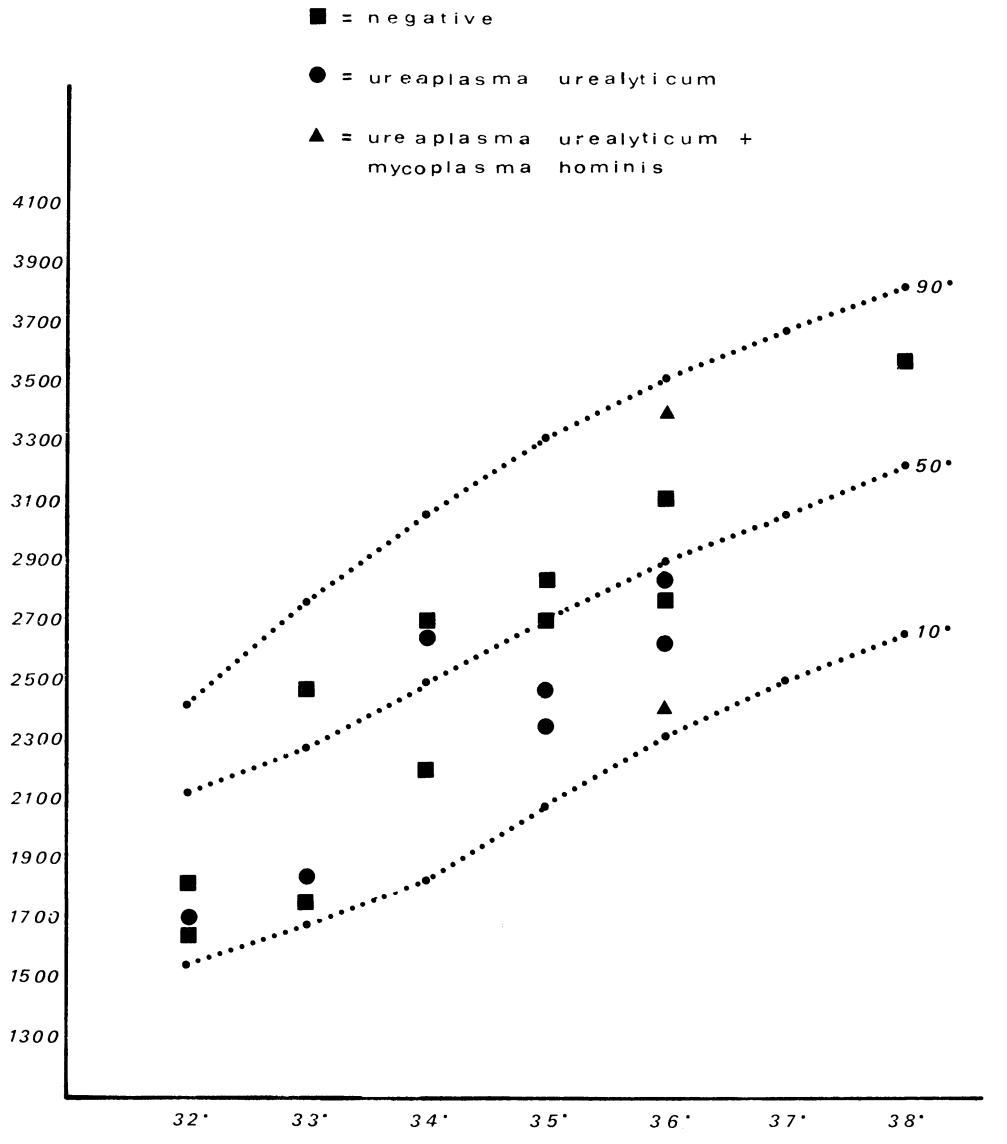

Fig. 1. — Birth weights in the 20 cases of premature membrane's rupture compared with the centiles of normal controls used in our Clinic.

in 18 % of the cases it was isolated with U. Urealyticum.

Always in Table 2 are reported, for the different categories of patients, the means (± SE) of the birth weights.

It must be pointed out how in 17 patients (34 %) with a positive research of U. Urealyticum, the mean (± SE) of the neonatal weights is higher than that of the 22 patients (44 %) with a negative vaginal research of mycoplasma.

The mean (± SE) of the birth weights of the 9 patients with a positive research of both M. Hominis and U. Urealyticum, results to be lower than that of the negative patients; a difference not statistically significant.

DISCUSSION AND CONCLUSIONS

The percentage of mycoplasma's isolation (M. Hominis and U. Urealyticum) in the vaginal exudate of the seventy pregnant women examined in our investigation, has resulted to be of 50%, not so different from that reported by some AA. as Mardh and Westrom [38], Romano et al. [39], Kundsin and Driscoll [13], Goedert et al. [40]. In agremeent with data reported in literature, M. Hominis has always been isolated with U. Urealyticum. The relative high frequency of mycoplasma's isolation during pregnancy, reported by different AA. and confirmed by our results, rises the hypothesis that these microrganisms can be considered as « pathogenous opportunists ».

Concerning the problem of the possible mycoplasmic aetiology in the premature membrane's rupture, our results (44 % of positive cases) disagree with those reported by Braun et al. [30] and by Kundsin et al. [13].

These AA. report percentages of isolation significatively higher in case of premature membrane's rupture, in comparison with controls at the same week of gestation.

Other AA. report data which confirm the absence of a significative difference in the percentage of mycoplasma's isolation between patients with premature membrane's rupture and controls [19, 40], being the percentage of isolation in patients with premature labour the same or, as in our series, lower than that of at term pregnancies.

In the 20 cases of premature membrane's rupture, the birth weights of the neonates have always ranged between the 10th and 90th centile of the controls' weights at the different weeks of gestation. This disagrees with DiMusto et al. [29] who thinks that, if the presence of mycoplasmas at vaginal level does not increase the incidence of premature membrane's rupture, however it can cause, by unknown mechanisms, a low weight at birth.

The low weight at birth is a problem which has been widely discussed, in particular after the reports of DiMusto et al. [29], Braun et al. [30, 41], Klein et al [28].

According to these AA. the positive research of mycoplasmas is the pathogenesis of the « small for date » infants.

Our results, obtained on 50 at term pregnancies, do not confirm this correlation, but on the contrary, while in the patients with positive research of U. Urealyticum the mean neonatal weight was of 3280 ± 320 (SE), in those with a negative research it was of 3130 ±250 (SE), that is lower.

Our data are confirmed by the recent assertion made by Barile (42), who has declared that we cannot talk of a mycoplasmic aetiology in the « small for date » till we will not prove the pathophisiologic mechanism of such a phenomenon. Such a conclusion has also been recently reported by other AA. [43]. In conclusion we can assert that:

1) eventhough mycoplasma's research in the genital apparatus, has resulted to be very useful for the treatment of both male and female sterility, in obstetrics

the isolation of such microrganisms seems to be limited to those cases of repeated abortion with unknown aetiology ([2]).

2) According to controversial data from literature, we think that the vaginal research of mycoplasmas during pregnancy has not to be considered a routine examination, till we will not have the certainty of a mycoplasmic role on the aetiology of the « small for date ».

3) No significative data have rised from our investigation, which support the hypothesis that the vaginal isolation of U. Urealyticum alone or with M. Hominis, increases the incidence or frequence of premature labours due to premature membrane's rupture.

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