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CHORIONAMNIONITIS, CHRONIC HYPOXIA, AND PATHOPHYSIOLOGICAL PRINCIPLES OF CARDIOTOCOGRAPHY

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ABSTRACT

The presence of severe antenatal hypoxia is common and in this case the fetus shows CTG abnormalities. Although many fetuses with cerebral hypoxic ischemic insults arising in the antenatal period may not demonstrate uniform CTG anomalies, nevertheless on the birth test some well-defined CTG characteristics can be identified that may appear in the subsequent intrapartum period.

The peculiar CTG pattern in this situation, with fetuses with pre-existing hypoxia or neurological damage, is characterized by a fixed and relatively non-variable baseline, with reduced or absent variability that does not demonstrate the presence of fetal cyclic activity. Sometimes a tachycardia may be present, usually much higher than 160 bpm, especially if the hypoxic insult is recent. In the case of a hypoxic insult with a more distant onset, however, the baseline appears normal (110-160 bpm). Contrary to the three CTG pictures mentioned above, associated with hypoxia that begins and evolves during labor, this CTG picture constitutes the demonstration of the presence of a stable encephalopathy that cannot be modified by any obstetric intervention, even aggressive ones. If the fetus suffers a further hypoxic insult after such damage or develops intrapartum hypoxemia during labor, decelerations in the fetal heart rate may appear in response to uterine contractions. These appear to have the characteristic of appearing small and superficial. In the absence of acidemia, the CTG does not show the presence of decelerations despite the brain damage. At birth, these children show an increase in red blood cells, a lengthening of the elimination time of erythrocytes, which suggests the possibility of antenatal hypoxic damage with the presence of multi-organ dysfunction, delayed onset of convulsions, damage to the cerebral cortex, presence of long-standing meconium-stained amniotic fluid, meconium aspiration syndrome, and pulmonary hypertension. In this situation there are many fetuses who present an IUGR, who may more easily develop acidemia and show a short-lived bradycardia with a rapid return of the fetal heart rate to baseline after having suffered the acute hypoxemic insult and a tachycardia with return to baseline for

increased sympathetic tone. An amniotized chorion can lead to generalized fetal inflammation, called Fetal Systemic Inflammatory Response Syndrome, which is produced, in part, by endothelial damage. This syndrome is associated with hypotension, neonatal seizures, mechanical ventilation of the newborn, meconium aspiration syndrome, multiple organ dysfunction, low APGAR at birth, neonatal depression, neonatal hypoxic ischemic encephalopathy, intraventricular hemorrhage with white matter damage, periventricular leukomalacia, bronchodysplasia pulmonary and cerebral palsy. Unfortunately, we do not have effective tools to diagnose these fetuses at risk of encephalopathy and infectious brain damage. CTG monitoring has low sensitivity in the detection of fetal systemic inflammatory response syndrome, placental inflammation or neonatal sepsis. When the infectious disease occurs isolated or associated with hypoxia, the following may be present: tachycardia, reduced variability, absence of fetal cyclic activity. However, none of these frameworks appear specific. Fetal tachycardia may be present without decelerations, and it seems that in such cases fetuses subject to infectious and/or inflammatory processes are more susceptible to even minimal hypoxic insults. In many cases the symptoms of infection and/or inflammation are not evident and the CTG pictures are non-specific. It appears important first to maintain a high level of suspicion and be aware that there are no reliable and predictive tools for diagnosing damage in an infected fetus. Although there is no evidence that cesarean section, in such cases of suspected or proven intrauterine infection with an uncertain temporal determination of fetal damage, is advantageous, however, especially if risk factors such as stained amniotic fluid, fever, CTG anomalies are present, IUGR, antepartum hemorrhage, it seems appropriate to resort to this operation and extract the fetus. In the case of fetal infection, it is necessary to avoid that intrapartum factors (prolonged labor, reckless use of oxytocin and uterine hyperstimulation, particularly traumatic vaginal operative birth) can aggravate the risk of brain damage. In such cases it is also necessary to avoid resorting to misleading means such as taking blood from the fetal scalp, STAN.

Keywords: Cardiotocograph; Chorioamnionitis; Cycling; Funisitis; Overshoots; Sinusoidal pattern; Zig Zag pattern.

Introduction

Chorionamnionitis represents the most common infectious complication during labor and delivery, affecting up to 6% of all pregnancies. This syndrome places both mother and fetus at risk for adverse outcomes. Maternal complications can be highly variable, including postpartum hemorrhage secondary to uterine atony, uterine rupture, urgent hysterectomy, endometritis, pelvic abscess, septic pelvic thrombophlebitis, sepsis, and intensive care unit admission. Infants from mothers with a diagnosis of clinical chorionamnionitis are at increased risk of low Apgar scores at 5 minutes, neonatal convulsions, neonatal sepsis, bronchopulmonary dysplasia, intraventricular hemorrhage, periventricular leukomalacia, need for mechanical ventilation, admission to the neonatal intensive care unit, and long-term infectious morbidity to neonatal death [1, 2].

Traditionally, clinical chorionamnionositis is diagnosed by the presence of maternal fever (defined by a body temperature ≥37.8°C or ≥38.0°C) and two or more of the following five clinical signs: maternal tachycardia (HR > 100 bpm), fetal tachycardia (FCF > 160 bpm), uterine pain, amniotic

fluid or purulent or foul-smelling vaginal discharge, and maternal leukocytosis (GB > 15000/mm3) [3]. Most cases of clinical chorionamnionitis are diagnosed in the intrapartum period (about 85%) [1].

The most frequently identified microorganisms in the amniotic fluid of patients with clinical chorionamnionitis are: Ureaplasma urealyticum, Gardnerella vaginalis, Mycoplasma hominis, Streptococcus agalactiae, Lactobacillus species, and Bacteroides species. Ascending microbial invasion represents the most frequent pathogenesis. However, alternative pathogenesis has also been proposed, such as hematogenous dissemination of microorganisms from the oral cavity or intestine, retrograde invasion from the peritoneal cavity through the Fallopian tubes, and accidental introduction of microorganisms during an invasive prenatal diagnostic procedure.

The literature has shown that the diagnostic accuracy of Gibbs' criteria is about 50 percent, this indicating the existence of several clinical conditions characterized by fetal and/or maternal infection and/or inflammation. A recent expert review clarified the concepts by providing the various definitions for these clinical conditions [4], which are listed below:

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cating the existence of several clinical conditions characterized by fetal and/or maternal infection and/or inflammation. A recent expert review clarified the concepts by providing the various definitions for these clinical conditions [4], which are listed below:

- Microbial invasion, which is the presence of microorganisms in amniotic fluid diagnosed by culture or molecular techniques on amniotic fluid taken by amniocentesis. This condition does not refer to the presence of inflammatory response.
- Intra-amniotic inflammation, i.e., presence of inflammatory response in the amniotic cavity, which can be diagnosed by observation of inflammatory cells (e.g., neutrophils) or increased concentration of inflammatory mediators (e.g., interleukin-6) or matrix metalloproteinases (MMP8).
- Intra-amniotic infection, which is the combination of microbial invasion of the amniotic cavity and intra-amniotic inflammation.
- Sterile intra-amniotic inflammation when intra-amniotic inflammation results unaccompanied by the presence of microorganisms.
- Acute histologic chorioamnionomyositis refers to the presence of neutrophils in the amniochorionic membranes or chorionic plate, an expression of maternal response.
- Funisitis or chorionic vasculitis, on the other hand, indicates inflammation of the umbilical funiculus and fetal vessels in the context of the chorionic plate and is representative of fetal response. In any case, the term "acute histologic chorionamnionositis" refers to a specific inflammatory lesion in which neutrophils are the predominant cells.
- Chronic chorioionamnionositis is characterized by the infiltration of lymphocytes, plasma cells, and macrophages and usually occurs at the time when infectious agents such as viral agents are present.

Maternal epidural analgesia fever

Approximately 20 percent of patients diagnosed with chorionamnionitis at term have no evidence of intra-amniotic infection on analysis of fluid obtained by amniocentesis, even though blood concentrations of cytokines are like those of patients with documented intra-amniotic infection [5]. The question that follows is what the origin of this systemic inflammatory response is. One possible answer is that many of these cases represent episodes of epidural-induced fever, an increasingly common occurrence given women's high use of this type of birth-analgesia especially in Western countries.

Considering that the epidural confers a 5-fold increased risk of fever compared with the population of pregnant women who do not use it, what might suggest a possible anesthesiologic origin of maternal fever is the rise in maternal body temperature within 4-6 hours after epidural catheter placement. Maternal epidural fever is a unique phenomenon observed in pregnant women in term labor, which, for example, is rarely observed when epidural is performed outside of labor. Increasing evidence suggests that such fever is inflammatory in nature. In fact, it has been shown that compared with women without epidurals, women with epidurals have an increased serum concentration of IL-6. In addition, the longer the duration of epidural analgesia the higher the concentration of IL-6 in maternal blood [6]. One possible explanation for the etiopathogenesis of such fever could be attributable to the use of local anesthetics, such as ropivacaine or

bupivacaine. Indeed, they could induce systemic inflammation after absorption through the epidural vascular network, which, moreover, is modified in pregnancy. It has been hypothesized that anesthetic diffusion occurs more readily in pregnant patients than in nonpregnant patients because of caval compression by the gravid uterus, resulting in congestion of the epidural venous plexus and reduced local free space. In contrast, a recent in vitro study has shown how ropivacaine is able to induce apoptosis of endothelial cells resulting in the release of mediators known as DAMPs (damage-associated molecular patterns) capable in turn of eliciting the production of pyrogenic cytokines IL-1β and IL-6, which could be a cause of maternal fever following parturition-analgesia [7].

Pathogenetic mechanisms of brain damage in fetal infection/inflammation

Infection in the fetus stimulates an immune reaction, known as fetal inflammatory response syndrome (FIRS), which can result in brain damage through various mechanisms. The major increase in pro-inflammatory cytokines and interleukins can exert direct damage through induction of neuronal apoptosis, or by disrupting the differentiation of neurons and oligodendrocytes during the process of active myelination. When fetal inflammation and/or infection occurs, the integrity of the blood-brain barrier is compromised, with increased permeability to inflammatory cells generated in peripheral tissues and other cytotoxic proteins. Such mediators exacerbate brain damage [8].

Pro-inflammatory cytokines in FIRS can activate microglia cells, which in turn release inflammatory and cytotoxic mediators, resulting in exacerbation of brain damage. Specifically, exposure to perinatal infection and inflammatory cytokines results in apoptosis of pre-myelinating oligodendrocytes. After apoptosis, the early precursors of oligodendrocytes, which had withstood the initial insult, proliferate more briskly; however, as they fail to complete maturation, they are unable to produce myelin. This results in increased susceptibility of the white matter to subsequent insults. Microglia cells play a central role in this process, as they release reactive oxygen species and excess glutamate, all of which are cell-damaging components [9].

Inflammation is a known worsening factor in the vulnerability of the fetal brain during labor and delivery. When the blood supply is limited, as during labor, the fetus tries to meet its metabolic needs by saturating hemoglobin with greater amounts of oxygen, conveying the blood supply to organs at greater risk of hypoxic insult, and limiting oxygen consumption. Thus, there is a slowing of the fetal heart rate, with increased myocardial oxygen extraction, and an increase in filling time in diastole resulting in greater telediastolic volume. This results in an increase in cardiac output, blood pressure, and redistribution of blood flow secondary to peripheral vasoconstriction leading to elective perfusion of the brain, heart, and adrenals.

Subsequently, the hypoxic-ischemic insult is followed by reperfusion of brain tissue, with a transient resumption of cellular metabolic functions. The moment the fetus also suffers an infectious-type insult, the storm of inflammatory mediators easily extends to the fetal brain, which represents a district subject to vasodilation by elective perfusion, thus promoting cellular damage.

The clinical counterparts on the fetal encephalon are heterogeneous; moreover, their severity de-

pends on the degree of fetal prematurity. They may be [9]:

- Hypoxic-ischemic encephalopathy
- Intraventricular hemorrhage
- Periventricular leukomalacia
- Perinatal strokes
- Cerebral palsy

In addition, infection in the fetus can also result after birth in meconial aspiration syndrome, bronchopulmonary dysplasia, hypotension, sepsis, multi-organ failure, and even death.

Cardiotocographic patterns in chorionamnionitis

Tachycardia

Absence of cyclicity

Reduced variability

Zig zag pattern

Uterine tachysystole

Reaction to scalp stimulation

Increased fetal heart rate

Since most histologic chorionamniosites are not recognizable by clinical examination, some Authors attempted to identify cardiotocographic (CTG) signs suggestive of chorionamnionitis. Galli et al. analyzed 2105 CTG tracings and identified 305 cases with an increased fetal heart rate baseline compared to the mean by gestational age or with a baseline during labor labor increased by 10%, in the absence of previous signs of hypoxia and maternal hyperpyrexia. Analysis of fetal outcome showed higher rates of Apgar score < 7 at 1 and 5 minutes, low pH in umbilical artery, and admission to neonatal intensive care unit in the group of fetuses with cardiotocographic signs suggestive of chorionamnionitis [10]. In chorioionamnionitis, the increase in baseline fetal heart rate is secondary to the release of inflammatory mediators which is also accompanied by an increase in the rate of fetal metabolism. The increase in baseline heart rate occurs in the absence of previous deceleration, unlike in intrapartum hypoxia, in which the fetus reduces its own heart rate in order to protect the myocardium, and subsequently increases it as a result of catecholamine release.

As pointed out by other Authors recently, the universally recognized cut-offs for defining a fetal heart rate as normal could lead the clinician to make the mistake of not recognizing chorionamnionitis. Considering that an increase in body temperature of 1°C corresponds to an increase in fetal heart rate of about 10%, it is estimated that about half of the infected fetuses at term gestation do not exceed 160 bpm, a cut-off considered still within the normal range. This obviously indicates the inadequacy of the normal range for fetal heart rate proposed by leading obstetrical scientific societies. Moreover, the same study showed that in histologically confirmed cases of chorionamnionitis, the increase in fetal heart rate baseline occurred in the absence of previous decelerations and almost always before the onset of maternal fever [11]. This in fact suggests that chorionamnionitis is first and foremost an infection of fetal origin that then spreads to the mother. Therefore, the clinician should get used to considering maternal fever as a late sign of chorionamnionitis.

Absence of cyclicity

Cyclicity is considered a fundamental feature of the integrity of the autonomic nervous system and the physiological interaction between the sympathetic and parasympathetic nervous systems. It consists of alternating periods with reduced and normal variability, thus reflecting the transition

from a behavioral state of active wakefulness to one of sleep.

The authors of a recent study analyzed 684 CTG tracings of single pregnancies with gestational age > 36 weeks, fetus in cephalic presentation, and pH in umbilical artery known. Absence of cyclicity was demonstrated in 5% of cases, and these cases were significantly associated with maternal hyperpyrexia (> 37.8°C) and Apgar score < 7 at the 5th minute. In addition, the analysis revealed an association between increasing baseline fetal heart rate and absence of cyclicity. However, about mode of delivery and umbilical artery pH < 7.05, no differences were found between fetuses with cyclicity and fetuses without cyclicity [12].

The absence of cyclicity in the presence of quantitatively normal variability should suggest the presence of both hypoxic and nonhypoxic causes of CNS depression. Possible nonhypoxic causes include metabolic, inflammatory/infectious (e.g., encephalitis), drug use (opioids), and structural abnormalities (e.g., brain malformations, fetal infarction). Fetal heart rate variability usually is reduced during fetal sleep, but if reduced for prolonged periods (i.e., more than 90 minutes) it could signify neurological depression from other causes. The reduced variability at high baselines should never suggest a period of sleep, precisely because during the normal sleep cycle the heart rate is normal or even lower in fetuses and infants. Here then, the absence of cyclicity in association with an increased fetal baseline heart rate and maternal hyperpyrexia could depose chorionamnionitis.

Reduced variability

Galli et al recently observed that one third of fetuses with histologically confirmed chorionamnionitis had persistently reduced variability [10] at CTG tracing.

However, recent evidence shows that during fetal compromise variability is subject to dynamic changes. This implies that reduction or suppression of variability is not always a sign of fetal compromise, just as an increase, albeit moderate, in variability does not automatically mean no fetal compromise [13]. Experimental animal studies have explored changes in fetal heart rate variability in infection.

In the sheep fetus, administration of high bolus doses of lipopolysaccharide is associated with increased variability and the appearance of mild decelerations. In contrast, in the experimental model in which chronic administration of small doses of lipopolysaccharide was interrupted by the administration of high bolus doses, a biphasic pattern of variability was observed, represented first by an increase and then by a reduction in variability [14,15]. Therefore, it can be concluded that the reduction in variability is not a specific cardiotocographic feature of chorionamnionitis.

Zig zag pattern

The zig zag pattern is characterized by an irregular upward and downward fluctuation from baseline with an amplitude of 25 bpm and a duration of at least 1 minute. It is distinguished from the jumping pattern, which is instead characterized by a baseline amplitude > 25 bpm lasting longer than 30 minutes. In a recent Finnish study, intrapartum CTG tracings of 5150 single pregnancies with gestational age greater than 33 weeks were retrospectively analyzed. The zigzag pattern was found in 11.3% of cases and only in pregnancies with gesta-

tional age greater than 37 weeks. In addition, three factors were independently associated with the zigzag pattern: male fetal sex, nulliparity and post-term gestational age [16].

Other authors demonstrated from retrospective analysis of 500 CTG tracings that the zigzag pattern during the expulsive period correlated significantly with low Apgar scores at 1 and 5 minutes, mild metabolic acidosis in the umbilical artery, and up to 11-fold increased ICU admission rate. The zigzag pattern is thought to be due to rapidly evolving hypoxia, which occurs, for example, during maternal pushing, or with repetitive decelerations with oxytocic infusion, or when uteroplacental oxygenation is reduced. In such a condition, the fetus does not have sufficient time to maintain its heart rate at baseline. At the same time, its sympathetic nervous system tries to increase the basal rate in order to get more oxygenated blood, while the parasympathetic system tries to reduce the heart rate in order to decrease the cardiac work. Such instability of the fetal autonomic nervous system leads to the zigzag CTG pattern [17].

Sukumaran et al. analyzed CTG tracings of chorionamnionitis cases at term gestation confirmed on histological examination. There were 25 cases identified clinically and later corroborated by histology; fetal heart rate baseline increase was found in 100% of cases, loss of cyclicity in 94% of cases, zigzag pattern in 70% of cases. This might suggest the fact that often, but not always, chorionamnionitis is associated with a hypoxic condition brought about by increased metabolic demand for the fetus. Therefore, fetal infection could lead to an accelerated drop in pH that finally results in the finding of metabolic acidosis at delivery [18].

Uterine tachysystole

In the study by Sukumaran et al in which 25 cases of chorionamnionitis were confirmed by histologic examination, tachysystole was observed in 82% of cases. This observation suggests that infection may irritate the myometrium through the action of inflammatory mediators. Therefore, the presence of increased frequency of uterine contractions in association with the previously described cardiotocographic abnormalities increases the suspicion of chorionamnionitis [18].

Reaction to scalp stimulation

The same Authors demonstrated how in most cases of certain chorionamnionitis the fetuses lost the ability to respond with acceleration of their heart rate to digital scalp stimulation [18].

Summary

In summary, CTG features suggestive for chorionamnionitis are as follows:

1. increased LB > 10% in the absence of previous deceleration and often before the onset of maternal fever
2. absence of cyclicity (especially if LB increased)
3. variability abnormalities are not CA-specific (decreased variability and zigzag pattern)
4. uterine tachysystole
5. absence of reaction to fetal scalp stimulation

Management

Standard treatment of chorionamnionitis involves administration of antibiotics and active management of labor labor by administering oxytocin or performing amniorexi and induction of labor for patients out of labor.

When intra-amniotic infection is suspected or diag-

nostically confirmed, the therapy recommended by the ACOG (American College of Obstetricians and Gynecologists) is ampicillin and gentamicin (ampicillin 2 g EV every 6 hours and gentamicin 5.g/kg every 24 hours). However, these antibiotics are not effective against Ureaplasma spp or Mycoplasma hominis. These bacteria have no cell wall, so beta-lactams (such as pennicillins and cephalosporins) and glycopeptides such as vancomycin are not effective as antimicrobial agents. Gentamicin is also not effective against Ureaplasma parvum and U. urealyticum. Recently, attention in the literature has focused on the use in chorionamnionitis of triple antibiotic therapy, which includes the following drugs: ceftriaxone, clarithromycin, and metronidazole. Such therapy has proven to be effective in eradicating intra-amaniotic infection by genital mycoplasmas and anaerobic/aerobic bacteria in preterm pregnancies. The rationale for choosing these antiobitics lies in their peculiarities: ceftriaxone has broad coverage for aerobic bacteria and a high rate of transplacental transfer, clarithromycin is effective against genital mycoplasmas, and metronidazole has excellent coverage against anaerobic bacteria [4].

Regarding the use of antipyretics in intrapartum maternal fever, the evidence is unclear. Paracetamol is usually administered to reduce maternal body temperature and the fetal tachycardia that usually accompanies it.

Clinical cases

Clinical case 1

Primigravida at 25+1 sg, 30 years old, BMI 42, admitted for threatened preterm delivery and suspected chorionamniosite. At the time of tracing, the patient had respiratory distress syndrome (RDS) prophylaxis with corticosteroids and was on tocolytic therapy with Atosiban ev, antibiotic therapy with Ampicillin and Gentamicin ev, and neuroprotection ev with Magnesium Sulfate. Subsequently, due to worsening maternal inflammatory indices and the appearance of maternal fever, it was decided to discontinue tocolytic therapy. There was then vaginal delivery of a live, viable fetus in cephalic presentation, weighing 820 g with Apgar of 1.4 and 6 at the first, fifth and tenth minutes of life, respectively, promptly intubated and transferred to the neonatal intensive care unit. Microbiological examination of the placenta was positive for Enterococcus faecalis.

In this case, the CTG is less informative than the overall clinical picture. The contractile pattern is poorly recorded for maternal habitus.

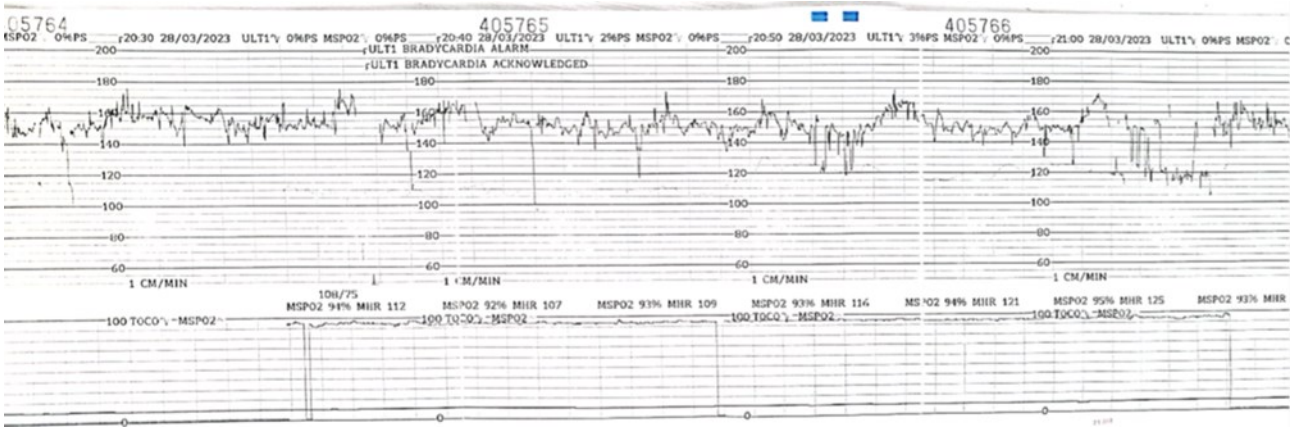

Figure 1: Normal CTG tracing with a baseline (LB) of150 bpm and preserved variability (ongoing tocolytic, antibiotic and ev neuroprotection therapy)

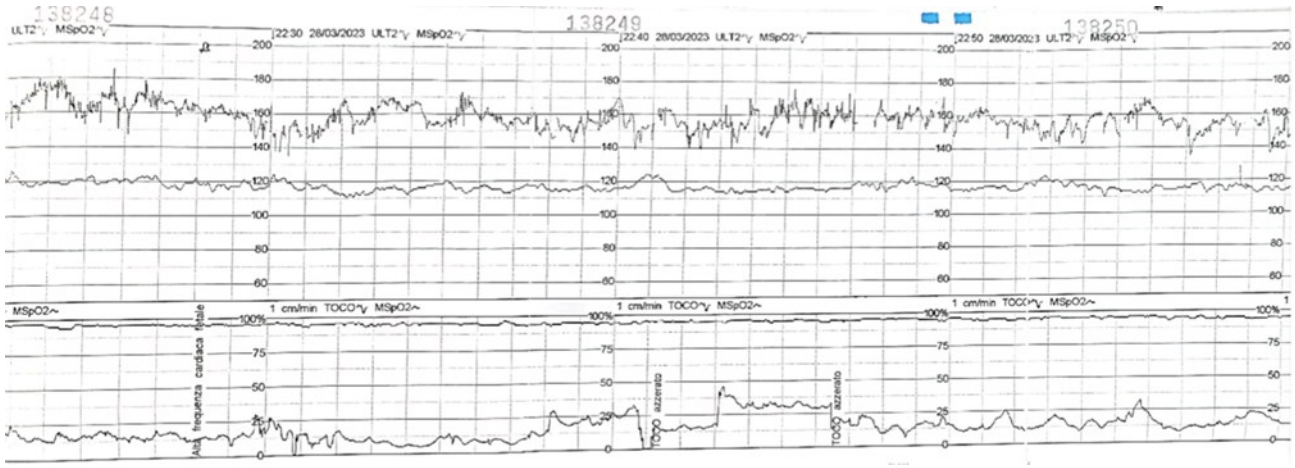

Figure 2: Fetal tachycardia (tocolytic therapy discontinued).

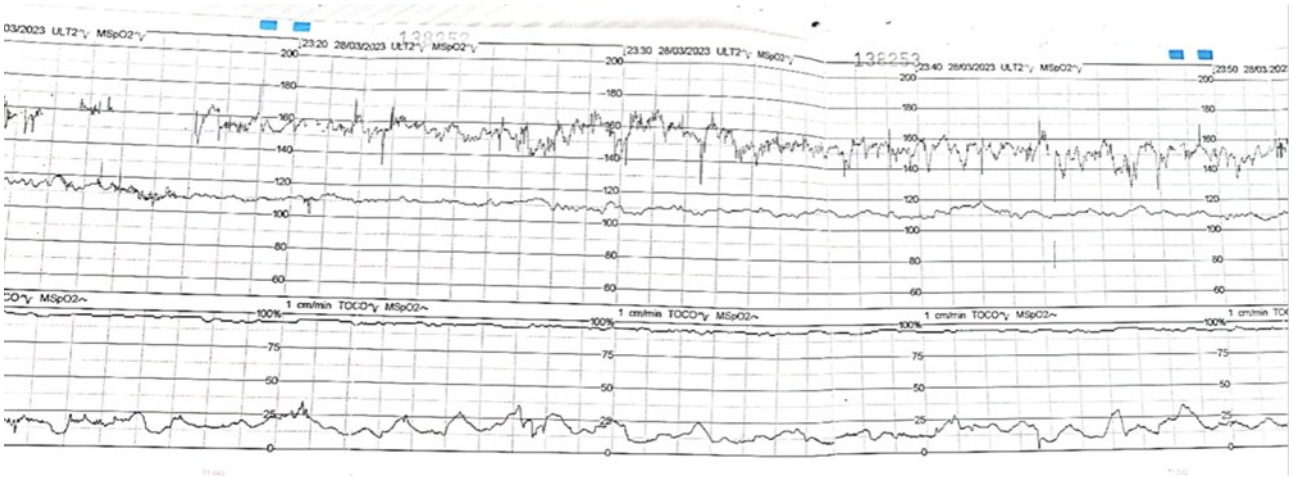

Figure 3: Fetal tachycardia and no cycling when also considering Figure 2

Case report 2

Secondigravida (previous term cesarean section) at 40+4 sg, 30 years of age, admitted for PROM (with a well-shortened posterior neck, pervious comfortably to 1 finger). Due to presence of intense uterine contractile activity one hour after admission, epidural analgesia was performed. At 8 hours, the patient presented with 3-4 cm cervical dilatation and fever (TC 37.8°C). Cesarean section is performed 4 hours later for CTG alterations and maternal hyperpyrexia. A female fetus is born, weighing 3930 g with Apgar 8 and 9 at the first to fifth minute, respectively. Microbiological examination of the placenta was positive for Mycoplasma hominis.

In this case, the CTG is more informative than the overall clinical picture.

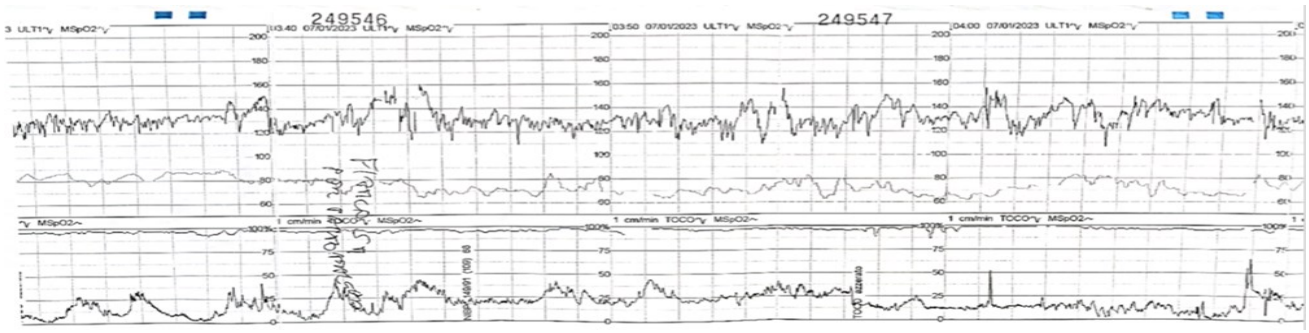

Figure 4: Normal CTG tracing

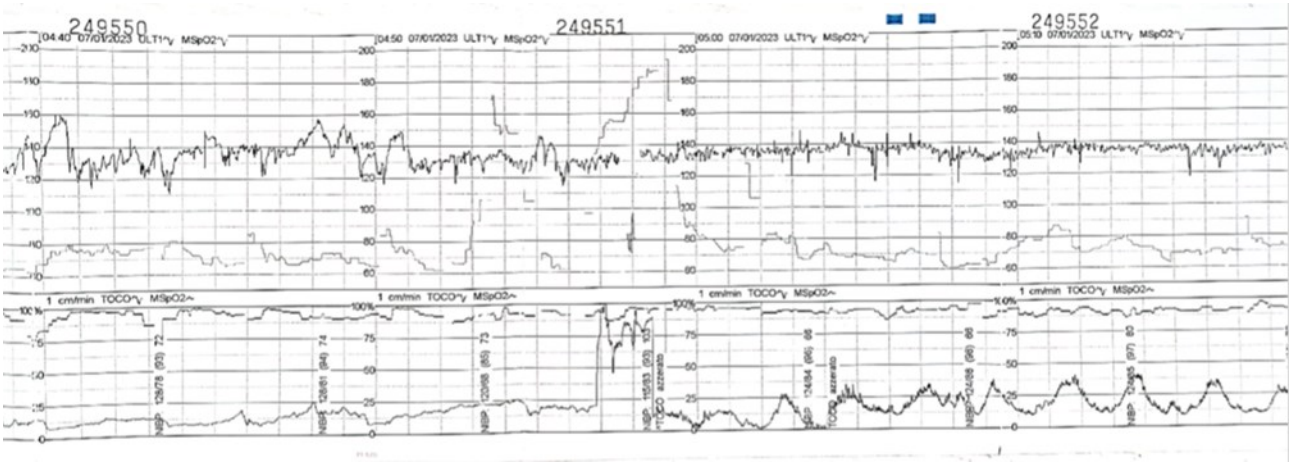

Figure 5: Normal LB (140 bpm), variability preserved, cyclicity preserved, accelerations present, decelerations absent. From 5:00 a.m. there is appearance of spontaneous tachysystole

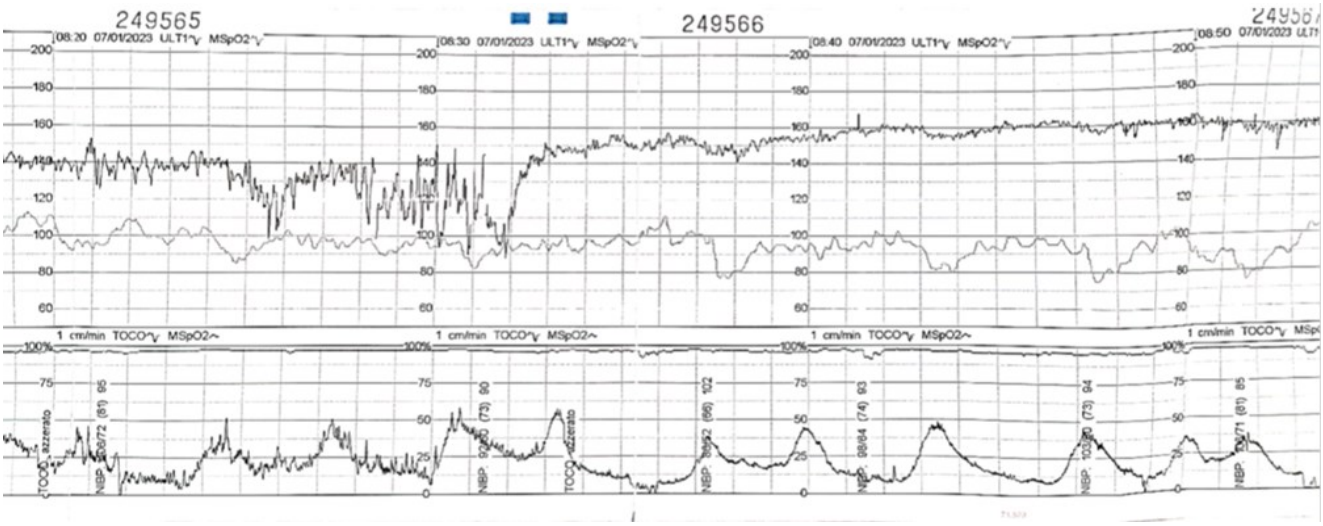

Figure 6: Spontaneous tachysystole persists, fetal tachycardia also appears

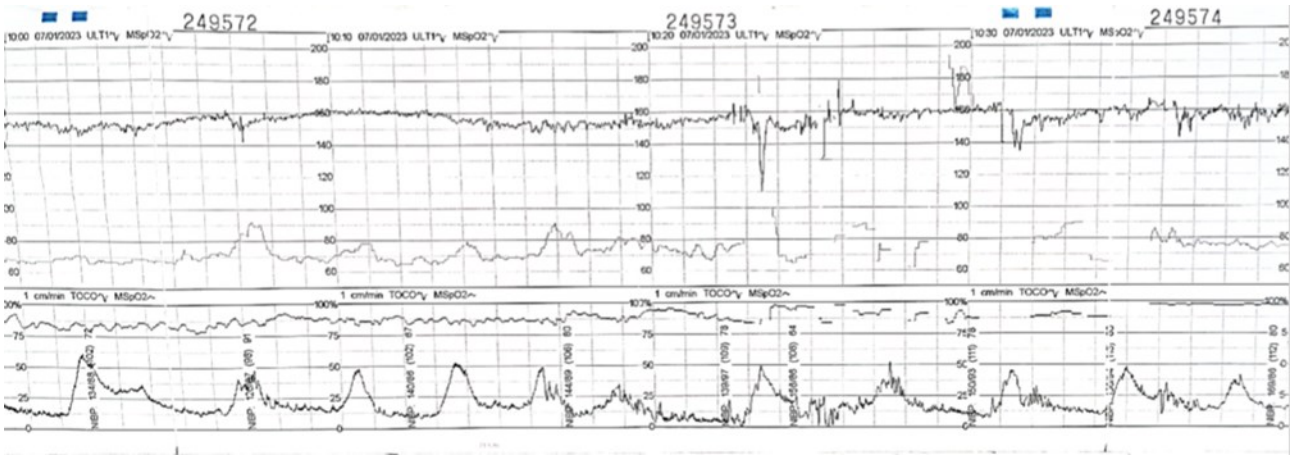

Figure 7: Tachysystole, fetal tachycardia (in the absence of previous decelerations) with reduced variability

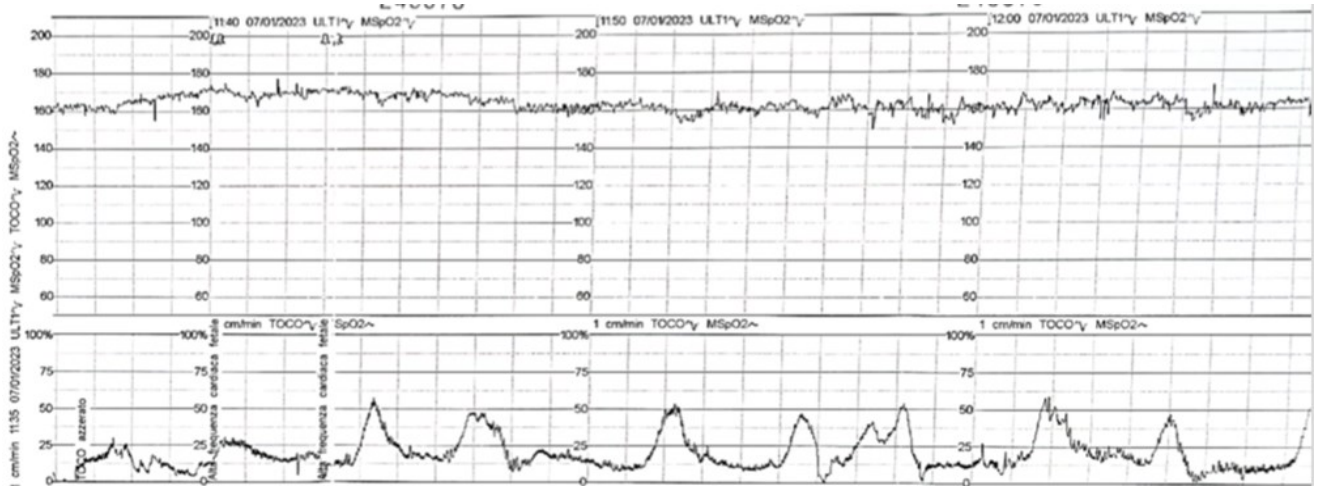

Figure 8: The loss of cyclicality is also confirmed at this point

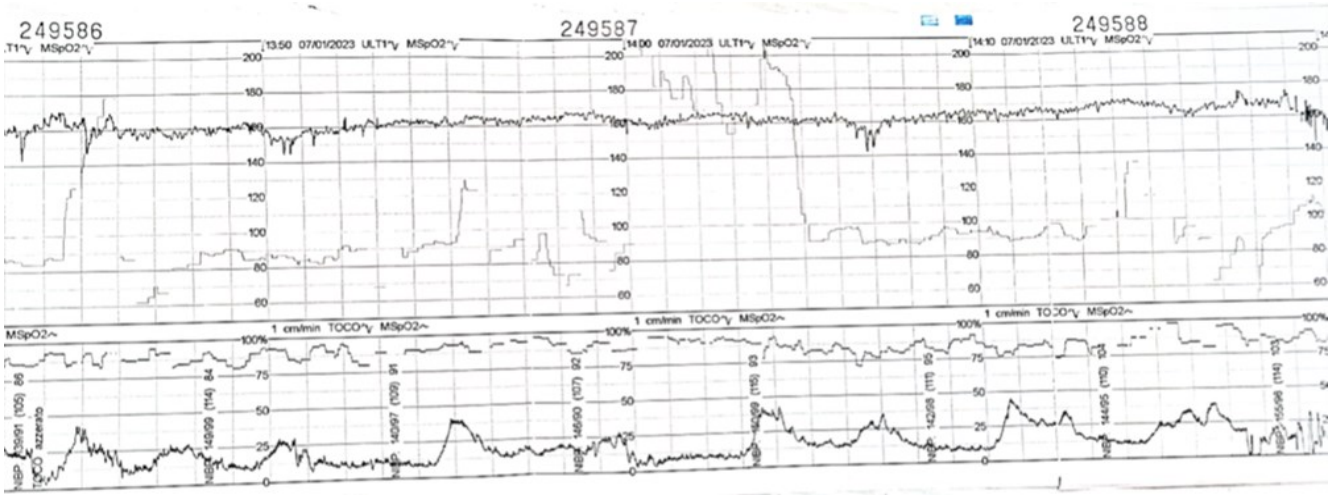

Figure 9: unchanged picture from the previous one (uterine tachysystole, fetal tachycardia, reduced variability, loss of cyclicity)

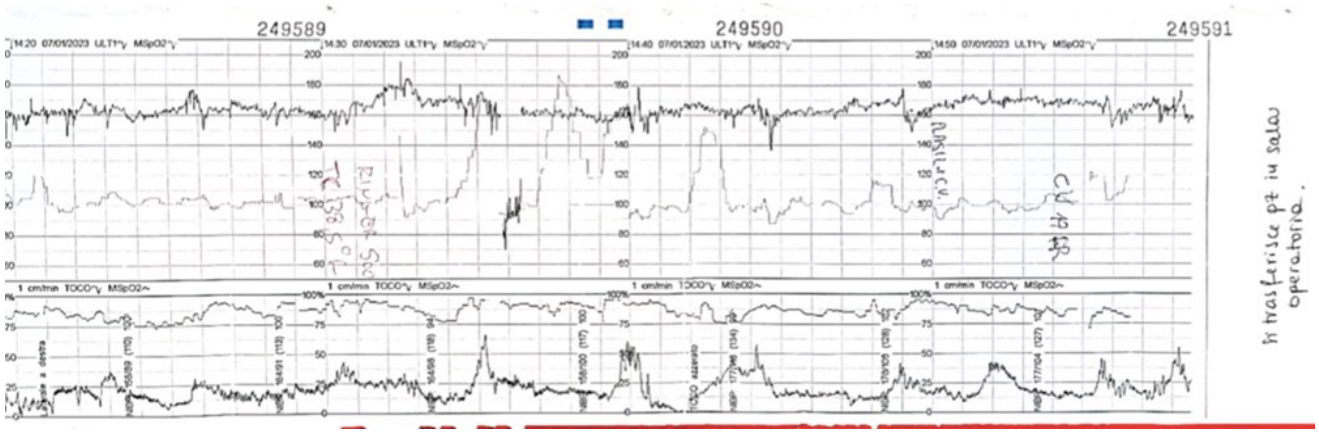

Figure 10: 6-hour CTG tracing with the same features: fetal tachycardia, reduced variability, loss of cyclicity, tachysystole.

Clinical Case 3

Ms. D.L. 35 years old.

Diagnosis on admission: III, II pregnancy at 32+5 weeks amenorrhea. IUGR.

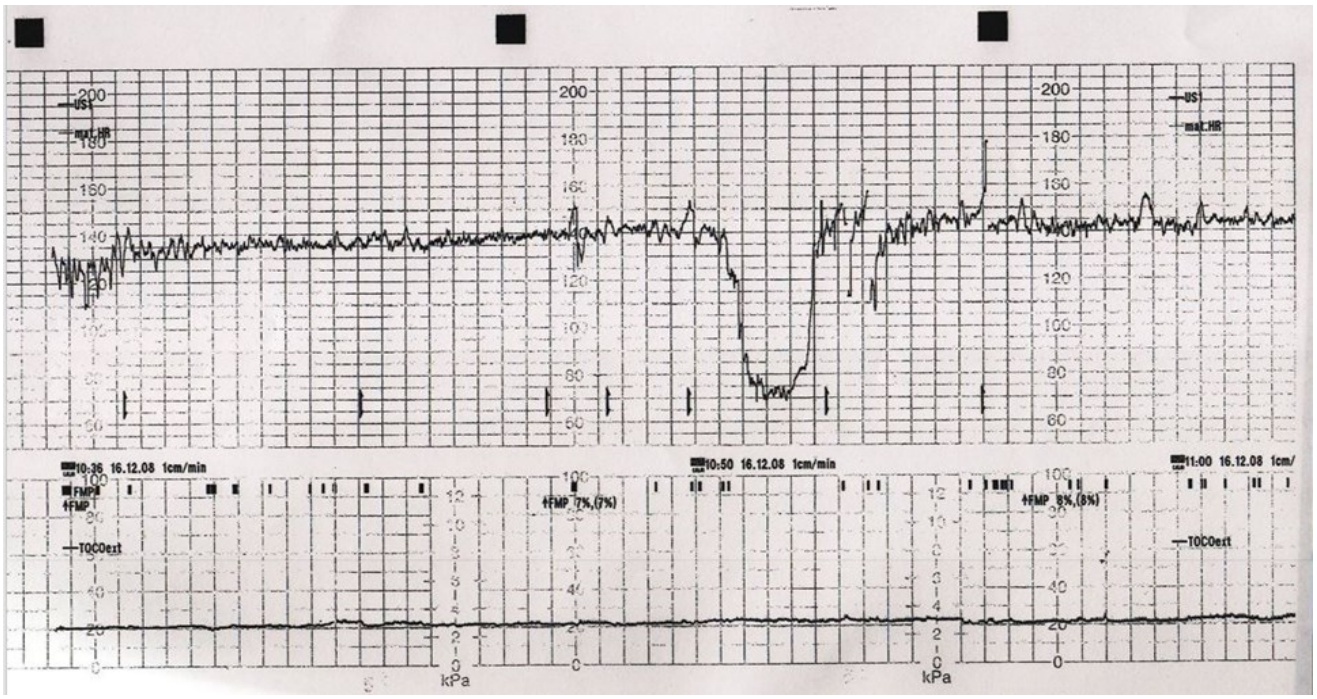

Figure 23.31

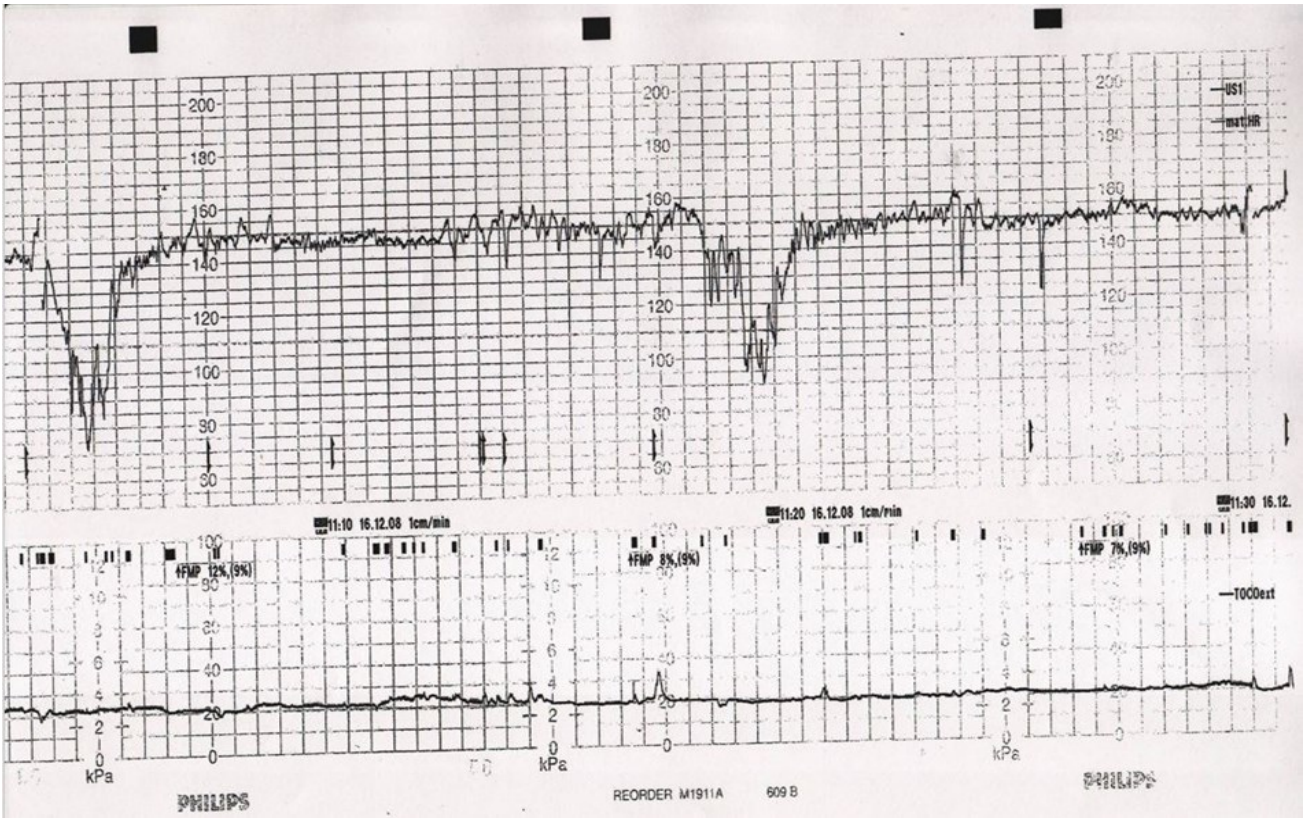

Figure 11

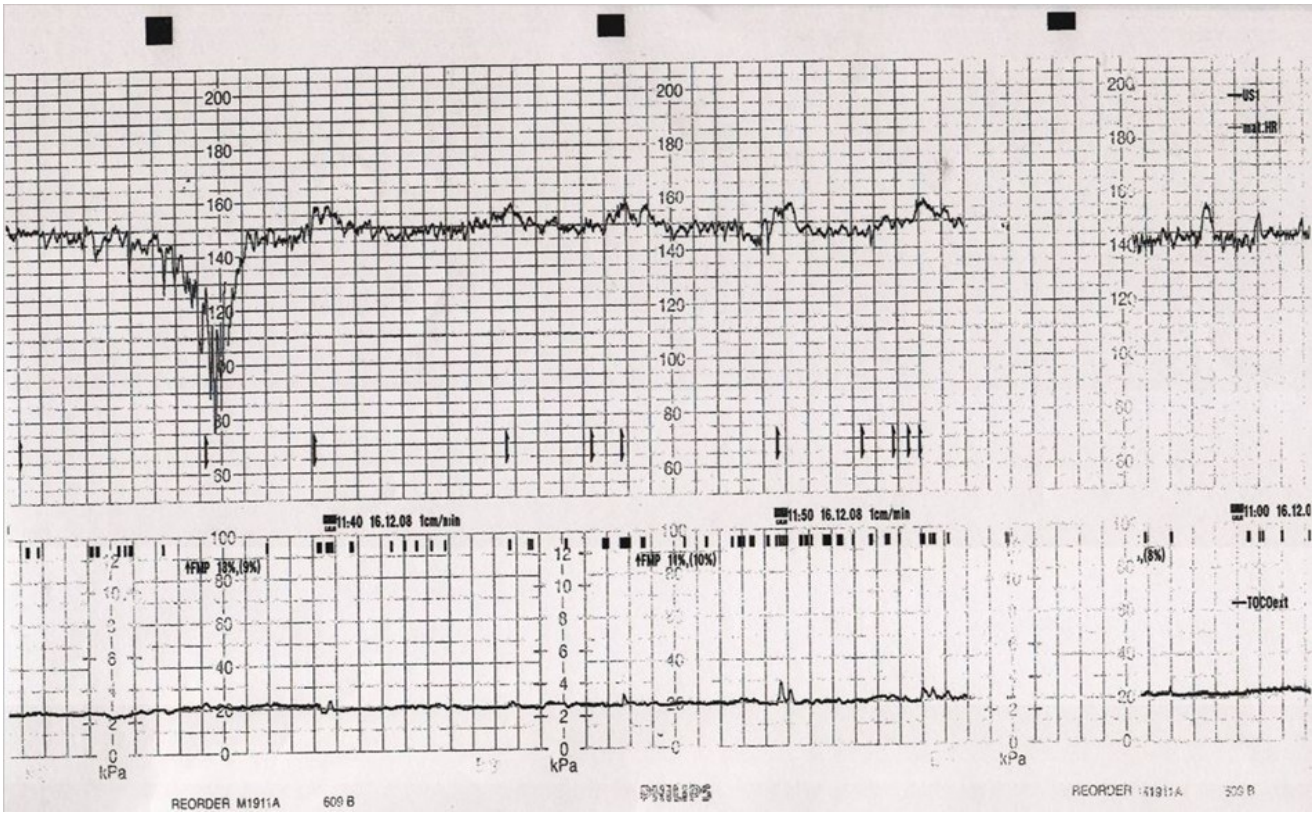

Figure 12

- 10:36 to 11:50 a.m. Figures 23.31-23.33
- CTG: chronic preexisting hypoxia in labor with reduced variability. Absence of atypical variable acceleration and deceleration indicative of subacute hypoxic superimposition on a preexisting chronic hypoxemic state.
- H 12:00 urgent cesarean section.

NEONATE

Male sex, weight 1250 g

Apgar: 1'-7; 5'-9.

Hemogasanalysis

- Artery: pH 7.1; pCO2 66.9 mmHg; pO2 8.5 mmHg; dBase -3.1 mmol/L.

Figure 13 Umbilical cord: length 34cm, maximum diameter 1.2cm, minimum diameter 1cm. Hyperspiralized.

Clinical Case 4

Ms. G.B. Age 33 years.

Diagnosis on admission: I pregnancy at 32 weeks of amenorrhea. Patient with chronic hypertension with superimposed preeclampsia on therapy. IUGR. PA 160/100

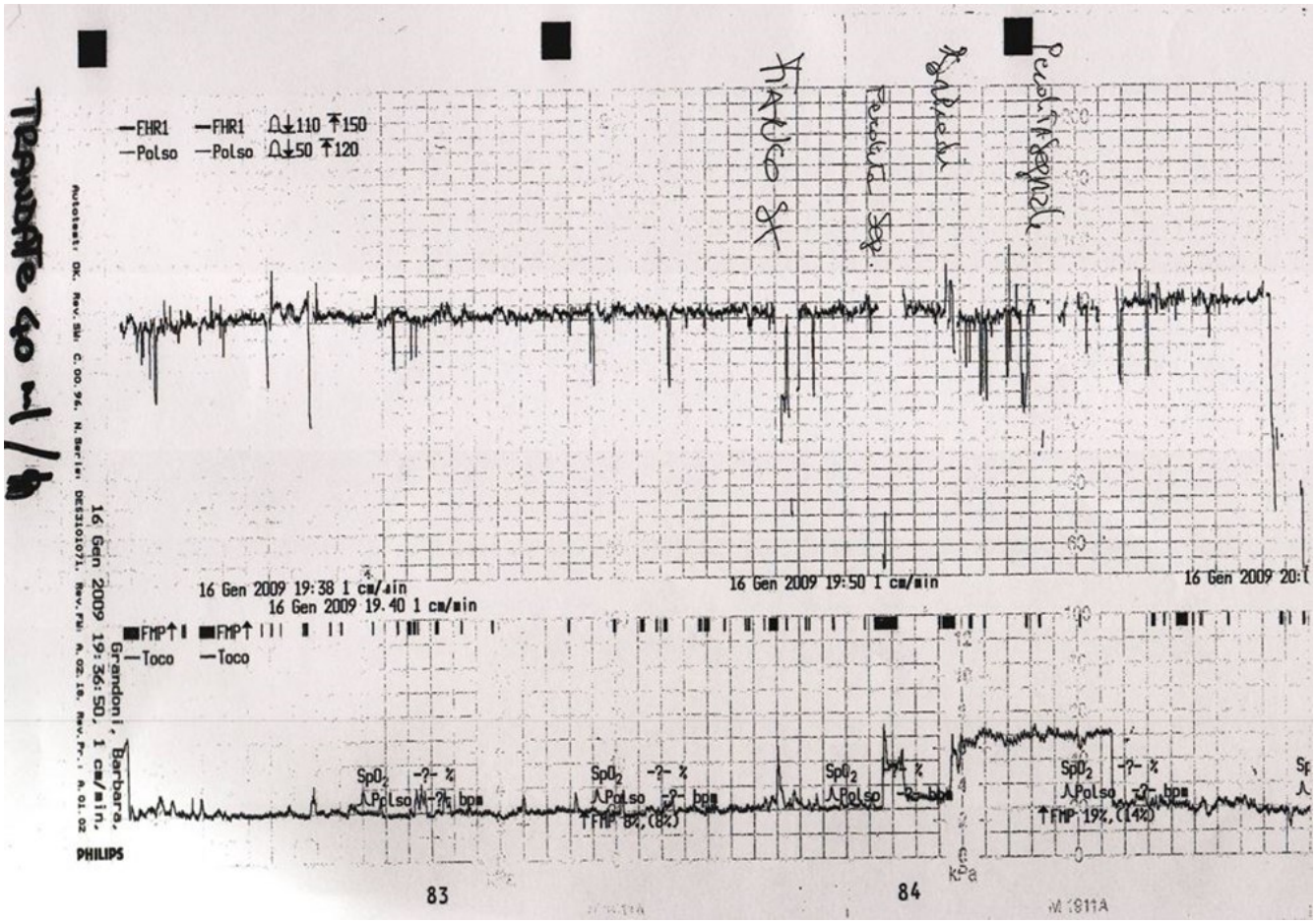

Figure 14

- h 7:30 pm to 7:50 pm. Figure 23.35
- CTG: Chronic hypoxia preexisting to pregnancy. Hyporeactive CTG with absence of variability and acceleration.
- h 20:00: Urgent cesarean section.

NEONATE

Male sex, weight 1,220 g.

Apgar: 1'-3; 5'-4

Hemogasanalysis

- Artery: pH 6.98; dBasi -14 mmol/L.

Metabolic acidosis and neonatal RDS.

Histological examination of placenta:

- Umbilical cord length 23 cm.
- Placenta weight: 268 g
- Diagnosis: dysmature placenta with relative deficit of terminal villi. Caliber of funiculus reduced.

Clinical Case 5

Ms. J.L. Age 27 years.

Diagnosis on admission: I pregnancy at 39+3 weeks of amenorrhea. Prodromes of childbirth labor.

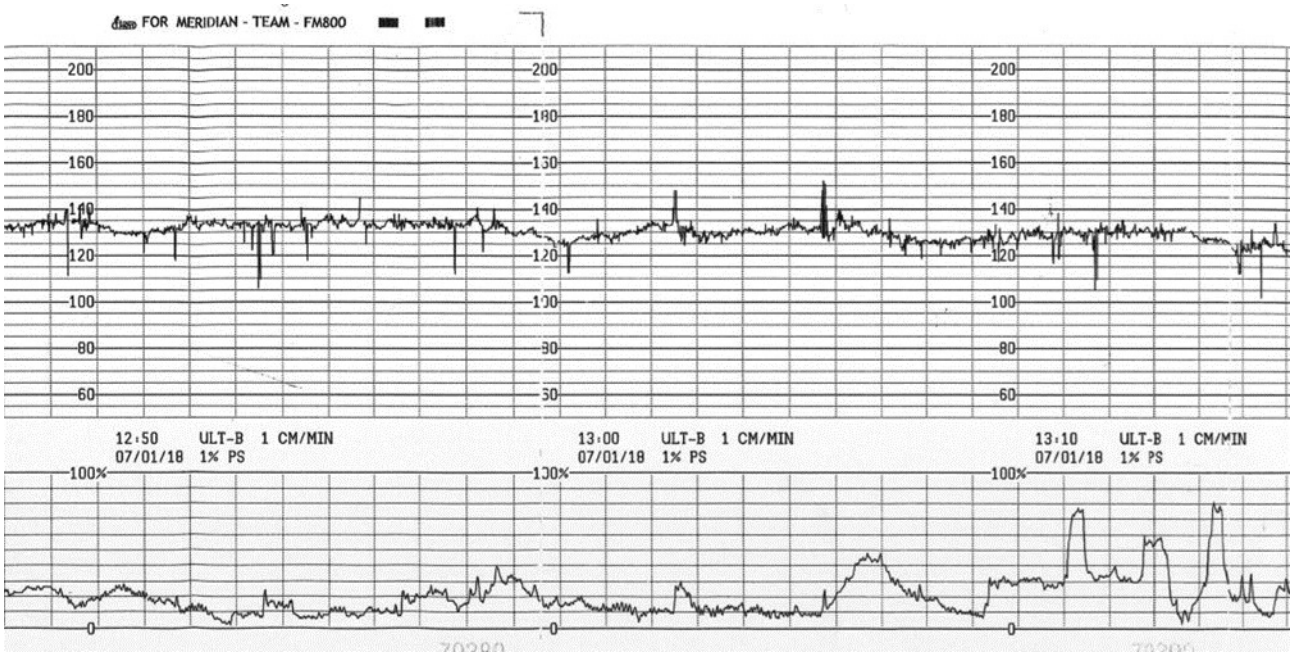

Figure 15

- Hours: 12:28 pm until 1:25 pm (Figure15)
- CTG: baseline 140, accelerations absent, variability reduced, typical of chronic hypoxia
- h 14:11, VO: regular vagina, uterine neck centralizing, shortened to 1/2, dilatation 3-4 cm, cephalic pp -2.

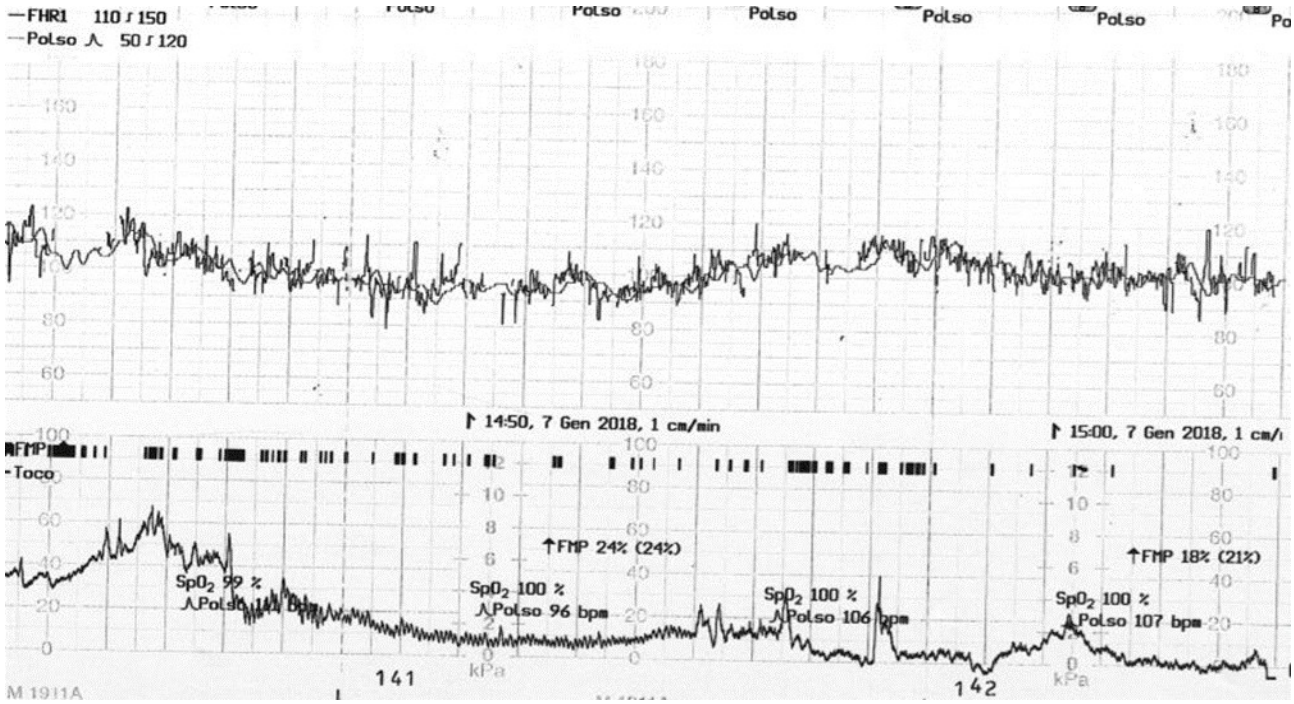

Figure 16

- 14:45 h Figure 16:
- CTG: Confirmation of previous CTG picture with baseline lowering and onset of severe bradycardia (90bpm).
- Doppler echo is performed with finding of bradycardia with no flow in diastole.
- h 15:15 Caesarean section is performed with extraction of male infant sex, dead, weight 4kg.

NEONATE

Male sex, weight 3,950g

Hemogasanalysis

- Artery: pH 6.7; pCO2 118 mmHg; pO2 3.8 mmHg; dBase -20.3 mmol/L.
- Vein: pH 7.1; pCO2 43.0 mmHg; pO2 133 mmHg; dBasi -13.6 mmol/L.

Comment: presence of pre-existing chronic hypoxia on admission so it appears vital to avoid the onset of further hypoxic stress. After 60 minutes of hyporesponsive CTG it appeared appropriate to proceed with immediate extraction of the fetus. Caesarean section was performed about two hours later with extraction of fetus deceased in the peripartum period.

Autopsy: male fetus with body development as per 40th gestational week with mild signs of macrosomia. Voluminous isolated vascular neoformation a type of hemangioma liver with aspects of blood congestion, without aspects of rupture. Exfoliation tetracavitary heart with marked coronary artery congestion and lesions evolving ischemic infarcts. Congestion and multiorgan hemorrhagic extravasation most evident at adrenal, renal, thymic, pulmonary, and meningeal levels.

Morphologic features consistent with high-flow congestive heart failure. No additional visceral, skeletal, or episkeletal malformative changes.

HISTOLOGY

Macroscopic: weight 670 g. Numerous areas of ischemic distress occupying 60% of placental parenchyma.

Microscopic:

- Crowded villi, hypermature compared to age, irregular branching, presence of immature villi (features of "delayed placental maturation")
- thickened stem villus vessels
- terminal villi vessels congested, microangiosis.

Diagnosis: placenta with adaptive changes to chronic hypoxic state. Villi alterations compatible with even latent maternal dysmetabolic state.

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