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Diagnosis and Management of Chorioamnionitis: A Case Report and Short Review of Literature

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Abstract

Introduction: Chorioamnionitis is an unprecedented complication arising during labor and the intrapartum period which can lead to adverse outcomes in the mother such as sepsis and postpartum infections and the neonate such as stillbirth, neonatal sepsis, cerebral palsy, and delayed milestones with an increased NICU stay. Several studies have been done over the past years to study the pathophysiology and outcomes of chorioamnionitis. The current studies focus on the early recognition and management to prevent further complications.

Patient and methods: We want to discuss the case of a 23-year-old full-term antenatal mother who received successful multi-disciplinary treatment at a tertiary care hospital and also discuss the literature available on basic pathophysiology, diagnosis, complications, and management of chorioamnionitis.

Results: The patient had a follow-up on an OPD basis with her baby 1 month post-operatively, both stable and healthy with no complaints.

Conclusion: An early clinical diagnosis with prompt initiation of antibiotics can lead to good outcomes for the mother and the baby.

Keywords: Chorioamnionitis, Fever in pregnancy, Sepsis, Peripartum infections, Pyrexia in pregnancy, Intra-amniotic, Premature rupture of membranes

Abbreviations: APGAR: Appearance, Pulse, Grimace, Activity, and Respiration; BP: Blood Pressure; CTG: Cardiotocography; CRP: C-Reactive Protein; IAI: Intra-Amniotic Infections; ICD: International Classification of Diseases; INR: Internalized Normal Ratio; LSCS: Lower Segment Cesarean Section; NICU- Neonatal Intensive Care Unit; NST: Nonstress Test; OPD: Out-Patient Department; PGE2: Prostaglandin E2; PROM: Premature Rupture of Membranes; PTL: Pre-Term Labor; PT: Prothrombin Time; AST/ALT: Aspartate Aminotransferase/Alanine Aminotransferase; TSH: Thyroid-Stimulating Hormone; WBC: White Blood Cells

Introduction

Chorioamnionitis is an infectious disease that can cause sepsis in pregnancy which could be life-threatening to the mother and fetus. Intraamniotic infection, also called chorioamnionitis, is an infection resulting in inflammation of the amniotic fluid, placenta, fetus, fetal membranes, or decidua, and any combination of the above. Chorioamnionitis can be attributed to ruptured fetal membranes where ascending infection, usually polymicrobial is common. In rare cases where

intact membranes are seen, small organisms like *Ureaplasma* and *Mycoplasma* can be isolated [1]. Not many studies have provided recent statistics, but nearly 16% of pregnancies are complicated by chorioamnionitis in a developing country like India [1]. Maternal mortality is rare, but nearly 4% of the term neonates have adverse complications and the chances increase exponentially in a preterm neonate [1]. This condition requires immediate recognition and comprehensive management. Provisional diagnosis has to be made through clinical signs and symptoms since the final diagnosis can be made only as per histopathological examination. Treatment includes injectable broad-spectrum antibiotics and eventually termination of pregnancy for a better outcome.

Case

A 23-year-old woman, belonging to a rural background, housewife and educated until 9th grade was a primigravida, who presented at 39 weeks of pregnancy with complaints of watery discharge per vaginum for the past 24 hours, She had been referred from a peripheral hospital with persistent fever and premature rupture of membranes of more than 24 hrs. She came to us as a sick-looking patient, with a fever of 38.4 C, moderate pallor, and signs of dehydration, her pulse was 124 beats/minute, respiratory rate was 20 breaths per minute, and blood pressure (BP) was 120/70 mmHg. On per abdomen examination, she had an extremely tender abdomen, full-term gestation, fetal heart rate was 174 beats per minute. On per speculum examination, she had meconium-stained foul-smelling liquor. On per vaginum examination, she was 2 cm dilated, 30-40% effaced, absent membranes, cephalic presentation, and station at |-2|. She had no significant medical or surgical history. She had no addictions to alcohol or tobacco and no allergy to any previously taken drugs.

Venipuncture sampling was done and all her blood investigations were sent. Her complete blood count by automated cell analyzer method was done, which revealed her hemoglobin of 8.2 g/dL, total white blood cell (WBC) count was 25700 per cc, neutrophil count was 92%, lymphocyte count was 3%, eosinophil count was 3%, and raised CRP of 49.19 (done by immunoassay method). Renal and liver function testing was done by fully automated testing and revealed serum creatinine of 0.7 mg/dL, urea levels of 17.2 mg/dL, sodium of 135 mEq/L, potassium of 4.12 mmol/L, serum bilirubin of 0.4 µmol/L, and AST/ALT of 36/34. Her blood group (done by forward and reverse grouping) was B negative and the Indirect Coombs test (by semi-automated agglutination testing) was found to be negative. PT/INR (done by semi-automated method) was 14.5/1.04; and the septic bundle including- Malaria- IgM (rapid antigen kit testing), Widal (tube method testing), dengue-NS1 and leptospira-IgM (both by ELISA automated method) came to be negative along with the COVID Rapid Antigen (using nasopharyngeal swab sampling) which was also negative.

She was started on broad-spectrum antibiotics for gram-positive and gram-negative coverage which included injectable cephalosporins (1 gm ceftriaxone twice daily and injectable metronidazole 100 ml thrice daily) and fluid resuscitation (500 ml normal saline and 500 ml ringer lactate), and injectable antipyretics (1 gm paracetamol) but fetal tachycardia (180-200 beats per minute) along with the maternal fever of 102 degrees Fahrenheit persisted for about four hours despite giving her antipyretics. Because of high clinical suspicion of chorioamnionitis, a decision for termination of pregnancy was made. The patient and her relatives were counseled regarding the high possibility of intraamniotic infection and the need for the termination of pregnancy. Induction of labor was done with dinoprostone gel instillation in the posterior fornix of the vagina under all aseptic precautions after counseling the patient and her relatives and taking informed written consent for the same. Post induction fetal heart rate monitoring yielded persistent fetal tachycardia (180-200 beats per minute) with a pathological non-stress test (NST) showing absent beat-to-beat variability with no accelerations over 90 minutes. A senior consultant's advice was sought and an emergency cesarean section was planned after taking written informed consent for the same.

Pre-operatively, a high vaginal swab was taken, and vaginal betadine douching was done under all aseptic precautions. Intra-operatively, findings included foul-smelling thick meconium-stained liquor along with friable decidua with adherent placental membranes. Injectable oxytocin 20 units in 500 ml ringer lactate was started immediately after delivery of the baby despite which uterine tone was not achieved, hence 10 units of oxytocin and methylergonovine injection 0.2 mg was given intra-muscularly as well. Uterus tone was flabby despite uterotonics and hence modified B lynch sutures were taken with a straight needle using Vicryl no 1 suture. Simultaneously intra-myometrial injection of Carboprost 230 microgram was given near the fundal region. A uterine cavity swab was taken and sent for culture and sensitivity. Placenta with cord sent for histopathological examination for confirmatory diagnosis. Intra-operatively, the patient had a total blood loss of 700 ml excluding the placenta and received 350 ml of blood (one unit) and 600 ml of intravenous fluid including normal saline and ringer lactate along with 200 ml of crystalloids (0.45% normal saline). A healthy male baby was born weighing 3 kg with a good APGAR score of 8 at one minute and 9 at five minutes of birth.

The patient was shifted to the general ward for post-operative monitoring and started on higher injectable antibiotics (Piperacillin-tazobactam 4.5gm thrice daily) and analgesics (injectable paracetamol 1 gm and ketorolac patches 20mg/patch, each lasting for 24 hours) with 100 ml of intravenous ringer lactate and normal saline per-hourly for the first 24 hours. In the immediate postoperative period, the patient had persistent tachycardia ranging between 110-124 bpm, and fever spikes ranging between 38-38.4 degrees

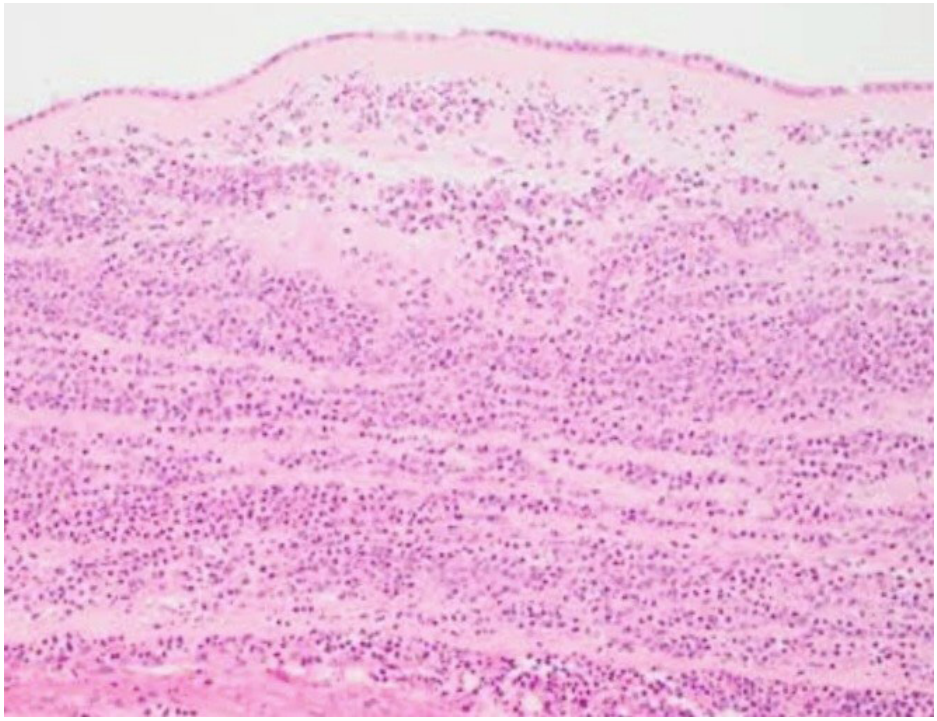

Figure 1: Histopathological picture of acute chorioamnionitis, neutrophilic infiltration through the layers suggesting acute infection of the amnion and the chorion.

Celsius. Day 2 post-operative investigations were sent, blood counts showed hemoglobin as 10.2 g/dL, total white blood cell count was 21500 (neutrophils 90%), and platelet count was 3.27 lac.

Uterine cavity swab was collected with the help of a sterile swab stick and its culture was done on chocolate, blood, and Mac Conkey agar isolated *Enterococcus species* sensitive to Penicillin/Azithromycin/ Vancomycin, hence the patient was continued on injectable Piperacillin, and oral Azithromycin 500 mg once a day per orally was added. Betadine vaginal pessaries were added along with antiseptic vaginal douching daily. Microscopic histopathological examination of the chorion and amnion was suggestive of acute inflammatory cell infiltrate suggesting chorioamnionitis (**Figure 1**). Blood cultures (venipuncture sampling) and urine culture sensitivity (using midstream clean catch urine sample) were done on chocolate and Mac Conkey agar came out sterile. Her 2 D echocardiography done due to persistent tachycardia turned out to be a normal study. Baby blood group (venipuncture sampling) was B positive, so injection Anti D 300 mcg was given on Day 2 post LSCS intramuscularly in the deltoid. The fever spikes continued for 3-4 days post-operatively and slowly improved with injectable antibiotics over 5-6 days.

She was discharged on day 13 post-operatively after complete suture removal and followed up after a month, healthy and asymptomatic. The baby was immunized completely appropriate for the age group, was on exclusive breastfeeds, and was doing well.

Discussion

Definition of chorioamnionitis

The World Health Organization (WHO) defines peripartum infections as any genital tract infection which occurs at any time between the onset of rupture of membranes, during labor, and day 42 in the post-partum period along with two or more defining factors- pelvic pain, pyrexia, abnormal foul-smelling vaginal discharge or uterine sub-involution [2]. The WHO's International Classification of Diseases ICD-10 and ICD-11 has assigned O41.12X as "Chorioamnionitis" and JA88.1 as "Infection of amniotic and its membranes," respectively [2]. Whereas the American College of Obstetricians and Gynecologists defines chorioamnionitis as an infection of the amniotic fluid, placenta, fetus, membranes, or decidua with resultant inflammation [3]. The National Institute for Health and Care Excellence (NICE) guidelines for preterm labor mentions premature rupture of membranes as a risk for intrauterine infection [4].

Incidence of chorioamnionitis

A study done on North Indian females by Arora et al. in 2015 revealed the incidence of chorioamnionitis to be 16% which

turned out to be similar to the statistics in other developing countries as well [4]. No recent studies have commented on the worldwide statistics regarding intraamniotic infections (IAI) and the disparity between the statistics between clinical chorioamnionitis and histological chorioamnionitis has led to further debate regarding the need for a revised set of guidelines for the diagnosis of chorioamnionitis.

Pathophysiology of chorioamnionitis

Intra-amniotic infection is most commonly caused by a combination of anaerobic and aerobic organisms. Once bacterial colonization starts, bacteria can not only infect the fetus but also can release endotoxins that, in sufficient quantities, can start an inflammatory response that may result in premature rupture of membranes (PROM), and preterm labor (**Figure 2**), and neurologic damage in the fetus. It is theorized that the bacterial endotoxins trigger a cytokine release in maternal and fetal tissue that leads to a release of additional cytokines, migration of leukocytes, and prostaglandin release from the myometrium and fetal membranes. This prostaglandin release can lead to rupture of the fetal membranes and/or to the initiation of uterine contractions, which is believed to be the primary cause by which intra-amniotic infection is a direct cause of preterm labor [5]. As per a study done by Zackler et al., the responsiveness of the uterine receptors to oxytocin is decreased in cases of clinical chorioamnionitis. In support of these findings, *in vitro* studies

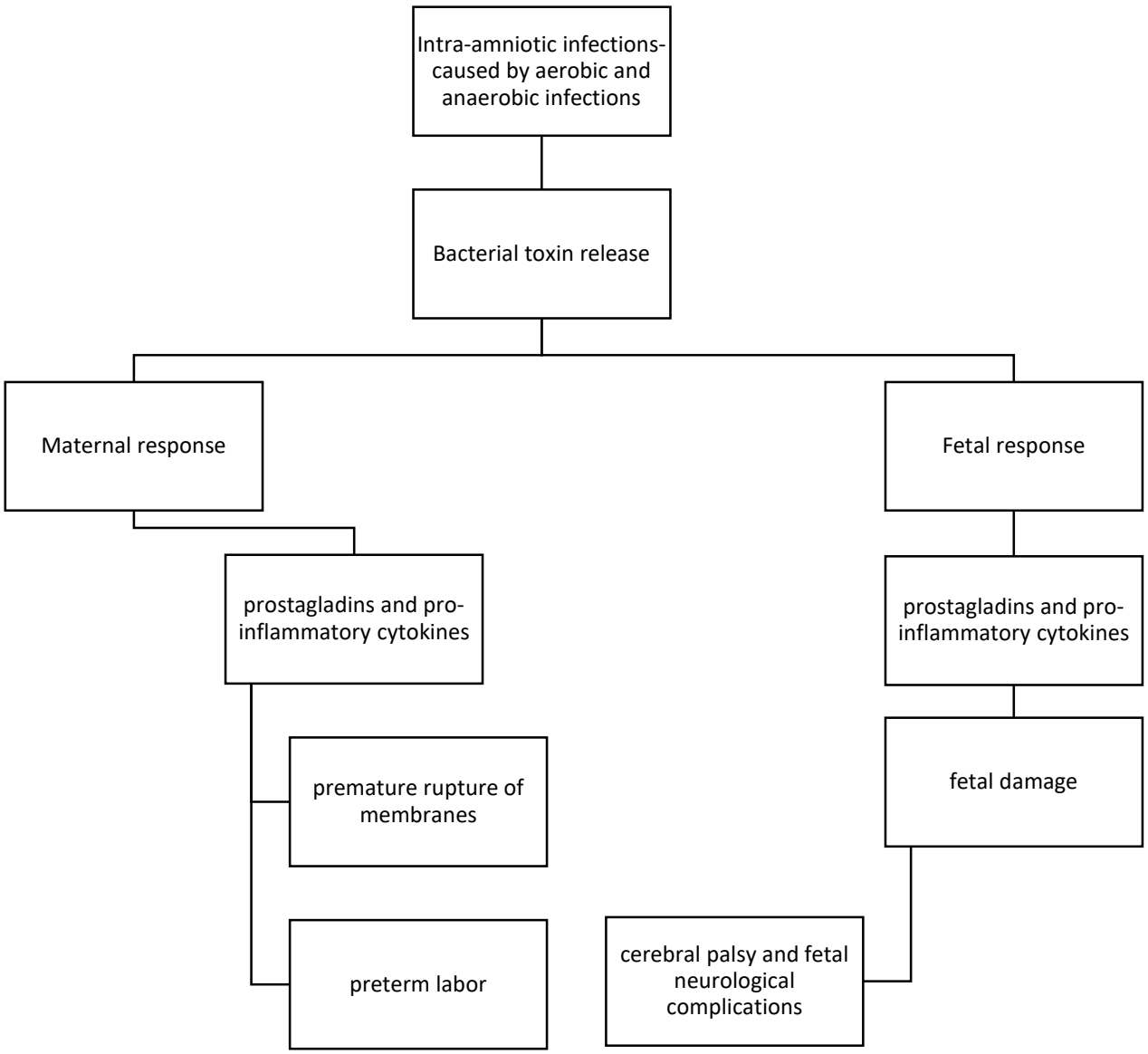

Figure 2: Pathophysiology and mechanisms of action of chorioamnionitis/intra-amniotic infections [5].

showed that the bacteria causing chorioamnionitis, such as anaerobic *streptococcus species*, *Veillonella species*, *Bacteroides species*, and *enterococcus faecalis*, reduce the contractility of the myometrium and its responsiveness to oxytocin infusion during the period of decreased contractility [6]. In support of these findings, intraoperatively during the cesarean section, our patient had uterine atony not responding to oxytocin infusion so intra myometrial carboprost injection was administered and modified B lynch sutures were taken. In our case, the species isolated in culture reports were *enterococcus* sensitive to azithromycin.

Clinical features and symptomatology of chorioamnionitis

The diagnosis of IAI (chorioamnionitis) is commonly made based on clinical symptoms, particularly the presence of maternal fever of more than 100.4°F (when there are no other identifiable reasons for fever) which may be accompanied by other symptoms like -maternal tachycardia (>100–120 beats per minute), fetal tachycardia (>160 beats per minute), uterine tenderness, purulent vaginal discharge or foul-smelling liquor and maternal leukocytosis (cells >15,000–18,000/mm^3) [6]. In our case, a suspected diagnosis of chorioamnionitis was established as the patient had presented with febrile episodes with maternal and fetal tachycardia (110-130bpm and 160-180 bpm respectively) along with meconium-stained, foul-smelling liquor and leukocytosis of 25,600 cells/mm^3. The inflammatory process is often asymptomatic and is described in only about 0.9–10.5% of pregnancies before the presentation of the clinical signs [8].

Laboratory tests and diagnosis of chorioamnionitis

According to NICE guidelines, a combination of clinical assessment and tests is used to diagnose intrauterine infection in women with premature rupture of membranes which include C reactive protein which is most commonly done laboratory test but this may be raised in any form of infections or fever of other causes and is of low specificity. We had a raised CRP of 49.19. Another nonspecific test is the white blood cell count showing maternal leukocytosis which is considered a criterion for diagnosing clinical chorioamnionitis, it was 25,600 cells/mm^3 in our case. Fetal heart rate monitoring using cardiotocography may show tachycardia which was also seen in our case, persistent despite intravenous maternal hydration [7].

Tests on amniotic fluid, usually obtained by amniocentesis, have been used for diagnosing chorioamnionitis. Amniotic fluid cultures are the most reliable test but are of limited use because culture results may not be available for up to 3 days. Some obstetricians use amniocentesis to confirm clinically suspected IAI to determine whether or not preterm termination of pregnancy is needed to avoid having an iatrogenic preterm birth. However, the value of this practice, because of its invasive nature, has recently been questioned [1]. Due to the non-availability of resources and being invasive, this test was not performed in our case.

Antibiotic regimens used in chorioamnionitis

As per a study conducted by Conde et al. regarding the management of chorioamnionitis, the first-line antibiotics for the treatment of clinical chorioamnionitis is ampicillin with gentamicin, which should be initiated during the intrapartum period. In the event of cesarean delivery, patients should receive clindamycin at the time of umbilical cord clamping [9].

Newer studies were done in low-resource settings in the North- Indian population by Venkat et al., which showed that among women delivering by cesarean delivery who were treated for chorioamnionitis, additional antibiotic therapy with cephalosporins decreased the risk of postpartum infection and primarily surgical site infection as compared to the current recommendations for antibiotics [10]. In our case, due to paucity of resources in a government setup, the patient was administered injectable broad-spectrum antibiotics (injectable ceftriaxone 1 gram twice daily) in the intrapartum period and continued on injectable piperacillin-tazobactam 4.5 gm thrice daily in the post-operative period.

Mode of termination of pregnancy in clinically diagnosed cases of chorioamnionitis

The American College of Obstetricians and Gynecologists Practice Bulletin on PROM has recommended that labor should be induced at the time of presentation, generally with oxytocin infusion, to reduce the risk of intra-amniotic infection in women with PROM at term [11]. In our case, we had given the patient a trial of labor with induction with intracervical PGE2 gel instillation but due to pathological CTG changes, a decision of cesarean section was taken for a better fetal outcome.

Histopathological diagnosis of chorioamnionitis

Both gross and histologic examinations are important to placental pathology when chorioamnionitis or intra-amniotic infection are suspected. Similar to a chronic immune-mediated inflammatory response during pregnancy and the histologic evidence of inflammatory cell infiltrates, bacterial infections typically present histologically as a local inflammation with acute neutrophil infiltration. In chorioamnionitis, these infiltrates will include the chorion, placental membranes, amniotic sac, and/or fetal membranes [12]. The histopathological examination of the placenta in our case showed acute chorioamnionitis (**Figure 1**).

Antibiotics administration to the neonate of a diagnosed case of chorioamnionitis

Once maternal chorioamnionitis is diagnosed, despite the duration of intrapartum antibiotics, the current

recommendation from the Center for Disease Control and Prevention (CDC), and the Committee on Fetus and Newborn of the American Academy of Pediatrics (AAP) requires a full sepsis workup and initiation of antibiotics treatment even in well-appearing infants. This increases neonatal exposure to antibiotics in an attempt to treat the rare possibility of early-onset sepsis. It is worth emphasizing that suspected chorioamnionitis without evidence of fetal infection is less likely to cause fetal or neonatal distress [13]. In our case, the baby was full term with no requirement of resuscitation at birth and a good APGAR score, he was observed closely for 48 hours for any signs of sepsis and no treatment/antibiotic regimen was initiated as the baby was doing well.

Strengths and Limitations of Our Study

The strength of our case lies in the prompt treatment initiated for the patient due to the high level of suspicion for chorioamnionitis clinically. The antibiotic regimen used in our case was injectable ceftriaxone and metronidazole pre-operatively as per the availability in our setup, but this regimen cannot be extrapolated to the general population as there are not enough studies supporting the same, which can be considered a limitation in our study. The diagnosis and the management of the case did eventually result in a healthy baby and mother which is the desired goal of every pregnancy.

Conclusions

Intra-amniotic infections demand a very high index of clinical suspicion because of serious complications like maternal septic shock and neurological deficits in the fetus. Hence prompt clinical diagnosis and early initiation of an appropriate antibiotic regimen are warranted. Termination of pregnancy can be individualized for better fetal and maternal outcomes.

Conflict of Interest

None by all authors.

Authors Contribution

G Bahuguna- Project development, manuscript writing; P Swain - Manuscript writing; A Anand - Manuscript editing; N Shaikh - Data collection; R Thatikonda - Data collection.

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