Secondary syphilis in the third trimester of pregnancy

Ryosuke Tajiri[1], Emi Kondo[1], Yuma Saito[1], Mao Sekimata[1], Yasuyuki Kinjo[1], Hiroshi Mori[1], and Kiyoshi Yoshino[1]

[1]University of Occupational and Environmental Health Japan

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Ryosuke Tajiri, Emi Kondo, Yuma Saito, Mao Sekimata, Yasuyuki Kinjo, Hiroshi Mori, Kiyoshi Yoshino

Facilities: Department of Obstetrics and Gynecology, School of Medicine, University of Occupational and Environmental Health, Japan

Iseigaoka, Yahatanishi-ku, Kitakyushu 807-8555, Japan.

Corresponding author: Dr. Ryosuke Tajiri

Department of Obstetrics and Gynecology, School of Medicine, University of Occupational and Environmental Health. Japan, 1-1 Iseigaoka, Yahatanishi-ku, Kitakyushu 807-8555, Japan.

Tel: +81-93-603-1611, Fax: +81-93-691-8892

e-mail:*r-tajiri@med.uoeh-u.ac.jp*

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Abstract:

Screening tests for syphilis are performed during early pregnancy in Japan. However, syphilis may develop after the second trimester, and remain undiagnosed due to the current screening methods. Moreover, no guidelines have been established for management of syphilis in the third trimester. We present the case of syphilis in the third trimester of a 32-year-old primipara female, which was managed successfully. Her early pregnancy screening tests were negative for syphilis. In the third trimester, she was diagnosed with second-stage syphilis. Treatment with penicillin G resulted in gross resolution of the ulcer and the skin rash. However, the risk of peripartum infection could not be ruled out. Therefore, caesarean section was performed at 38 weeks of gestation. Guidelines should be established for management of syphilis and mode of delivery during the second and third trimesters of pregnancy, which would aid in successful disease management and prevention of perinatal death or disability.

Key words: Cesarian Section/Pregnancy/Pregnancy Complications, Infectious/ Syphilis, Congenital

Introduction:

Syphilis is an infectious disease caused by *Treponema pallidum*(TP), a member of the Spirochaetaceae family. It is one of the most common sexually transmitted diseases. According to the World Health Organization (WHO) estimates, approximately 17.7 million people all over the world between the ages of 15 and 49 years had syphilis in the year 2012, and this number reportedly increases by an estimated 5.6 million every year (1). The estimated prevalence and incidence of syphilis varies with region and country. The highest prevalence of syphilis has been reported in Africa, with more than 60% of new cases occur in developing countries (1).

Gestational syphilis reportedly occurs most frequently in Africa, accounting for more than 60% of the global estimates (2). Syphilis is a Category 5 infectious disease in Japan according to the Infectious Diseases Law, and the number of syphilis cases has been gradually increasing since 2013 (3). Syphilis, especially among young people, has become a concern in the recent years. Syphilis in pregnant women and congenital syphilis have become public health issues worldwide (4). In Japan, the haematology test for syphilis is performed at public expense as a screening test in the first trimester of pregnancy during antenatal health examination. In some foreign countries, syphilis screening tests are also conducted in the second and third trimesters of pregnancy (5). However, in Japan, screening tests for syphilis are not conducted after the initial examination.

Herein, we report a case in which a vulvar ulcer at 37 weeks of gestation led to the diagnosis of syphilis after a negative screening test during early pregnancy.

Case report:

A 32-year-old primipara female was referred to our hospital for painless delivery. Prenatal history included one prior spontaneous miscarriage in a year ago. The patient had a history of smoking, which she had stopped after the discovery of pregnancy. She had a history of panic disorder and bipolar disorder, for which she was on medication. However, she self-interrupted her medication and hospital visits after discovering her pregnancy. Pregnancy was spontaneous and was managed at a primary care facility. The initial screening test performed at 12 weeks of gestation was negative for rapid plasma reagin (RPR) and TP antibodies. No abnormalities were observed in other laboratory results. At 22 weeks of gestation, she developed vulvovaginal and vaginal itching, which was diagnosed as vulvovaginal candidiasis by vaginal culture and treated with oxenazole vaginal suppositories. She was referred to our hospital at 33 weeks of pregnancy, which has a comprehensive perinatal mother and childcare centre, because she wanted to have a painless delivery. Thereafter, the patient continued antenatal care at the hospital. She had persistent vulvar itching and white tinea versicolor discharge. She continued the treatment for vulvar candidiasis with an oxazol vaginal suppository, but the treatment was refractory. At the time of her visit at 37 weeks and 2 days of pregnancy, painless induration and ulcerative lesions were observed on the vulva, and a blood test was performed on the suspicion of syphilis. Early in the morning of the next day, 37 weeks and 3 days after conception, she developed fever and pain during urination and was urgently admitted to the hospital on the same day.

On admission, the patient had a fever of 37.5°C. On examination, rice-sized erythematous plaques were observed on the palms, along with pale oedematous erythematous plaques with infiltrates on the right forearm and trunk, and numerous rice-sized painless ulcerative lesions on the vulva (Figure1). Internal examination revealed no bleeding or water breakage, and the cervix was closed. Uterine tenderness was not observed. Blood tests revealed a white blood cell count of 9000/μl (84.6% neutrophils); C-reactive protein (CRP), 10.47 mg/dl; PT, 13 s, and APTT, 64 s. Cardiotocography (CTG) findings on admission were 145 bpm at baseline, moderate baseline fibrillation, transient tachycardia, no transient bradycardia, and no uterine contractions. Transabdominal ultrasonography showed that the foetus was growing at a rate equivalent to the number of weeks. None of the findings were suggestive of congenital syphilis, such as obvious foetal hepatomegaly, ascites, foetal oedema, or placental thickening.

Based on positive RPR and TP antibodies, along with clinical symptoms, such as painless ulceration of the vulva and a generalized rose rash, she was diagnosed with second-stage syphilis. Subsequent detailed interviews revealed that her husband had used a sex establishment at around 15 weeks of gestation, and also had sexual intercourse with her during the same time. The patient's husband was treated with oral benzylpenicillin. After discussing the treatment plan with the Department of Infectious Diseases, the patient was treated for neurosyphilis with 4 million units of penicillin G six times a day for 10 days. The patient was in full-term labour at the time of treatment initiation. No Jarisch-Herxheimer reaction was observed. Although the generalized rosacea and vulvar hard chancre had resolved, the blood tests were positive for RPR and TP quantitative tests (RPR: 11.58 R.U. and TP antibody: 188.5 COI). No specific guidelines have been established for the mode of delivery in cases of syphilis diagnosed in the third trimester of pregnancy. Since the patient remained positive for RPR and TP antibodies, and the risk of peripartum infection could not be assessed, we opted for a caesarean section. An emergency caesarean section was performed under

spinal anaesthesia at 38 weeks and 3 days of gestation due to the onset of labour pain. A girl child weighing 2908 g, with an Apgar score of 8/9 and an umbilical artery blood pH of 7.280, was delivered. The first cry was rather weak, and prompt resuscitation was initiated. Since spontaneous respiration was weak, Continuous Postive Airway Pressure (CPAP) and oxygen were administered, after which the respiratory condition improved. Based on the maternal condition, the patient was admitted to the NICU for close examination and treatment of congenital syphilis. Blood test at birth showed a negative RPR of 0.49 R.U., positive TP antibody of 18.3 COI, and FTA-Abs-IgM of less than 5. Although there were no findings suggestive of congenital syphilis on physical examination, a dose of 50, 000 U/kg/dose of penicillin G was started after birth to prevent congenital syphilis. Vital signs of the new-born remained stable after the start of treatment. No obvious signs of infection were observed, and penicillin G administration was terminated on the 10th day of life. Early congenital syphilis test was negative, and the patient was discharged on the 19th day of life.

The mother continued postoperative penicillin G infusion until postoperative day 5, after which she was discharged. The patient is currently receiving treatment on an outpatient basis. Histopathological examination of the placenta revealed necrotizing funisitis (Figure 2). In addition, immunohistochemical staining for TP antibodies showed slightly positive organisms (Figure 2).

Discussion:

There is insufficient literature on delivery of pregnant women with syphilis. No specific guidelines have been established regarding treatment methods or modes of delivery in syphilis patients. Consequently, treatment policies and modes of delivery vary from one medical facility to another. We reviewed the literature on management of pregnancies complicated by syphilis that occurred in the third trimester of pregnancy.

Syphilis Treponema is a bacillus of the genus *Treponema* , with a width of approximately 100-200 nm and a length of 10-20 μm (6). It is a sexually transmitted disease that can be transmitted via contact with mucous membranes and skin (6). It is also known that untreated syphilis infection during pregnancy can lead to vertical infection and congenital syphilis in the child (6,7). Clinical manifestations result from a local inflammatory reaction caused by proliferating spirochetes in the tissues. In general, early syphilis refers to infections that can be sexually transmitted and is synonymous with infectious syphilis. The WHO defines early syphilis as infections of less than 2 years duration (8). Patients with first episode of syphilis present with a single chancre or multiple lesions at the site of genital or sexual contact and regional lymphadenopathy, approximately three weeks after infection (6). Secondary symptoms such as fever, headache, and maculopapular rash on the flanks, shoulders, arms, chest, and back appear. The rashes often involve the palms of the hands and the soles of the feet (6). Mother-to-child transmission primarily occurs during the primary and secondary infection periods, followed by the early incubation period (5,6,9). Infants born to infected mothers are often born premature, have low birth weight, and clinical signs that mimic neonatal sepsis (such as poor feeding, lethargy, rash, jaundice, hepatosplenomegaly, and anaemia)(10,11).

Majority of syphilis cases in infants occur due to in utero transmission, although mother-to-infant transmission of syphilis may occur at the time of delivery. Spirochetes have reportedly been detected in placental or umbilical cord samples as early as 9–10 weeks of gestation, which substantiates transplacental transmission to the foetus (12).

Syphilis often presents with diverse symptoms and is difficult to diagnose clinically. Painless lesions in hidden exposed sites, such as the cervix and rectum, are often missed. In addition, secondary syphilis eruptions and other lesions may appear hazy or could be mistaken for other diseases. Diagnosis of syphilis is often based on the medical history and the results of blood and other laboratory investigations. Serology is the most common method for diagnosing syphilis in both symptomatic and non-symptomatic individuals who are screened.

Screening for syphilis is universally recommended for pregnant women, regardless of previous exposure, because it is a highly effective preventive intervention against vertical transmission during pregnancy(5). Most national guidelines recommend screening for syphilis during the first antenatal visit, ideally during

the first trimester. Some countries recommend that high-risk women should be screened again in the third trimester of pregnancy and at the time of delivery to identify new infections.

In the present case, syphilis screening test in the first trimester of pregnancy was negative, but symptoms such as hard chancre confirmed syphilis infection in the third trimester of pregnancy. A detailed history after the onset of the disease suggested that she had sexually transmitted syphilis from her husband immediately before or after conceiving. Therefore, it was assumed that the initial screening test result was negative because of pre-infection or early infection. She was in full-term labour when the infection was discovered. Penicillin G infusion to prevent congenital syphilis was administered for 10 days, as per the package insert. The vulvar and skin lesions were confirmed to have disappeared. However, lesions on the vaginal wall and cervix were difficult to identify with the naked eye, and the possibility of trans natal vaginal infection could not be ruled out. Therefore, we elected to perform a caesarean section. There is no clear description of the mode of delivery for syphilis cases in late pregnancy in the guidelines, and this may be considered controversial. We also believe that screening for syphilis during the second trimester of pregnancy should be considered in the future.

In conclusion, we encountered a case of a pregnant woman with second-stage syphilis complication that developed in the third trimester of pregnancy. Incidence of syphilis has been on the increase among young people in the recent years, and we anticipate that similar cases may increase in the future. Therefore, it is desirable to establish guidelines for management and mode of delivery of patients with syphilis in the second and trimesters of pregnancy.

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Figure legends:

Figure 1. A. Rice-sized erythematous plaques on the palms. B. Pale oedematous erythema of the abdomen. C. Pale oedematous erythema on the back. D. Numerous rice-sized painless ulcerative lesions on the vulva.

Figure 2. A. Gross findings of the placenta and the umbilical cord. B. Necrotizing funisitis (H&E). Low power showing scattered inflammatory cells in the vessel wall. C. Necrotizing funisitis (H&E). Medium power showing scattered inflammatory cells in the vessel wall and an outer band of mild coagulation necrosis with cellular debris. D. Immunohistochemical staining for TP antibodies. High power showing slightly positive organisms.