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Rash in Pregnancy: Chickenpox

Gebede Döküntülü Hastalık: Suçiçeği

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Abstract

Chickenpox is an viral infection that is transmitted from person to person through direct contact with skin lesions or by inhaling respiratory secretions of infected individuals. Although it is usually seen in childhood, it can also occur rarely in adults. In adult population, serological tests are helpful in addition to clinical diagnosis. Viral infections with skin rashes can lead to more complications during pregnancy for both the baby and the mother. Therefore, vaccination against preventable diseases should be administered before pregnancy. In this article, a 29-week pregnant who was clinically compatible with chickenpox but developed seroconversion in the first month serologically was presented.
Keywords: Chickenpox, serology, pregnancy, rash

Öz

Suçiçeği, insandan insana çoğunlukla deri lezyonlarıyla direkt temas veya suçiçeği virüsü ile enfekte bireylerin solunumsal sekresyonlarının inhalasyonu yolu ile bulaşan döküntülü bir viral enfeksiyondur. Genellikle çocukluk çağında geçirilmekle birlikte nadir olarak erişkinlerde de görülebilir. Erişkinlerde klinik tanının yanı sıra serolojik tanı testleri yol göstericidir. Döküntülü viral enfeksiyonlar gebelikte hem bebek hem de anne için daha komplike seyredebilir. Bu nedenle aşı ile korunulabilecek hastalıklara karşı gebelik öncesinde aşılama uygulanmalıdır. Bu yazıda klinik olarak suçiçeği ile uyumlu olan ancak serolojik olarak birinci ayda serokonversiyon gelişen 29 haftalık bir gebe olgusu sunulmuştur.
Anahtar Kelimeler: Suçiçeği, seroloji, gebelik, döküntü

Introduction

Chickenpox infection is a highly contagious disease caused by the varicella zoster virus (VZV) and characterized by fever and rash. It is a DNA virus belonging to the *Herpesviridae* family. Like other herpesviruses, it remains latent in the sensory ganglia after primary infection. While primary infection is the varicella virus infection, latent infection causes shingles (herpes zoster) [1,2].

After the virus enters the conjunctiva or respiratory tract, it replicates in the nasopharynx and regional lymph nodes. Primary viremia occurs 4-6 days after infection and spreads to other body parts such as liver, kidney and sensory ganglia. This is followed by secondary viremia with skin lesions[1]. The virus is transmitted from person to person mostly by direct contact with skin lesions or by inhalation of respiratory secretions from infected individuals. Rarely, chickenpox may develop by direct contact with skin lesions of patients with disseminated herpes zoster or by inhalation of lesion fluids[2]. The incubation period is 14-16 days on average after contact (it can vary between 10-21). This period may be extended up to 28 days in patients receiving varicella zoster immunoglobulin (VZIG) as prophylaxis after exposure. Chickenpox typically presents with a generalized rash and fever, predominantly on the face and trunk, less commonly on the extremities. The lesions, which are initially observed as maculopapular, change in the form of vesicles, pustules and crusts within a few days. The vesicle stage is the most contagious stage. The disease is

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considered contagious from 48 hours before the rash appears until all lesions reach the pustular stage. Chickenpox infection usually causes a disease lasting 5-7 days in immunocompetent individuals. While it can present with mild symptoms and very few rashes, it is also possible to present with severe symptoms and more than 1.000 rashes. Chickenpox infection tends to be 25 times more severe in adults than in children. Varicella zoster virus pneumonia is particularly likely to occur in adults[3]. The lesions are extremely itchy, patients often scratch their lesions, which increases aerosol generation, increasing the risk of disease transmission[4]. However, even in patients in whom itching is completely avoided, spread from the lesions by aerosol occurs. Bacterial cellulitis, pneumonia and sepsis are among the important complications of the disease[5]. Among the central nervous system complications, two are very important. The first is cerebellar ataxia, which is usually self-limiting and is seen in 1 in 4,000 patients, and the second and more serious complication is encephalitis, which can be seen in 1 in 10,000 patients. Varicella zoster virus encephalitis can be severe and even fatal[6]. While chickenpox infection usually has only a single episode in a lifetime, there are also cases of reinfection reported in the literature[7]. The probability of severe varicella infection and VZV pneumonia occurring in pregnant women is 10-20% higher than in adults who are not pregnant[8]. Factors that increase the likelihood of varicella pneumonia occurring in pregnant women include primary infection occurring in the third trimester, smoking, and having more than 100 skin lesions[9]. In this article, it was aimed to present the follow-up and treatment of a patient with chickenpox who presented with rash and high fever at 29 weeks of pregnancy, whose first serological tests were negative and who developed seroconversion after the rash disappeared.

Case Report

A 37-year-old patient with a 29-week-old twin pregnancy without any known chronic disease was admitted to our center with rashes that started a week ago and spread to the whole body in 2-3 days, and a fever that started the day before and increased to 38.1 °C. There were erythematous-appearing vesicular lesions around her body, commonly accompanied by itching, stinging, and burning, including the scalp and genital area (Figure 1). It was learned that the patient, who described myalgia and severe weakness, did not remember whether she had chickenpox in her childhood and had not been in contact with anyone who had a rash recently. It was learned that VZV IgM, cytomegalovirus IgM and rubella IgM tests performed two days ago were negative. The patient with suspicious chickenpox infection was admitted to the ward for further examination and treatment.

In the system examination, no pathology was detected except vesicular lesions on the erythematous background, predominantly distributed in the scalp, trunk, genital region and proximal extremities, and umbilical vesicles around the umbilicus. In the hemogram, leukocyte count was 12070/µl, neutrophil count was 78%, Hb level was 9.1 g/dl, platelet count was 195000/l, AST 44 U/l, ALT 22 U/l, creatinine 0.53 mg/dl, CRP 18.7 mg/l (n=0.5), sedimentation rate was 50 mm/hour and INR was 0.99. In the complete urinalysis, there was no significant finding except mild proteinuria. The patient was consulted to the obstetrics and gynecology clinic, no abnormality was found in the vital signs of both fetuses, and routine obstetric controls were recommended. The serological test results were as follows: VZV IgM (-), VZV IgG (-), EBV VCA IgM (-), EBV VCA IgG/EA (+), EBV EBNA IgG (+), anti rubella IgM (-), anti rubella IgG (+), measles IgM (-) and measles IgG (-). Antiviral treatment was not

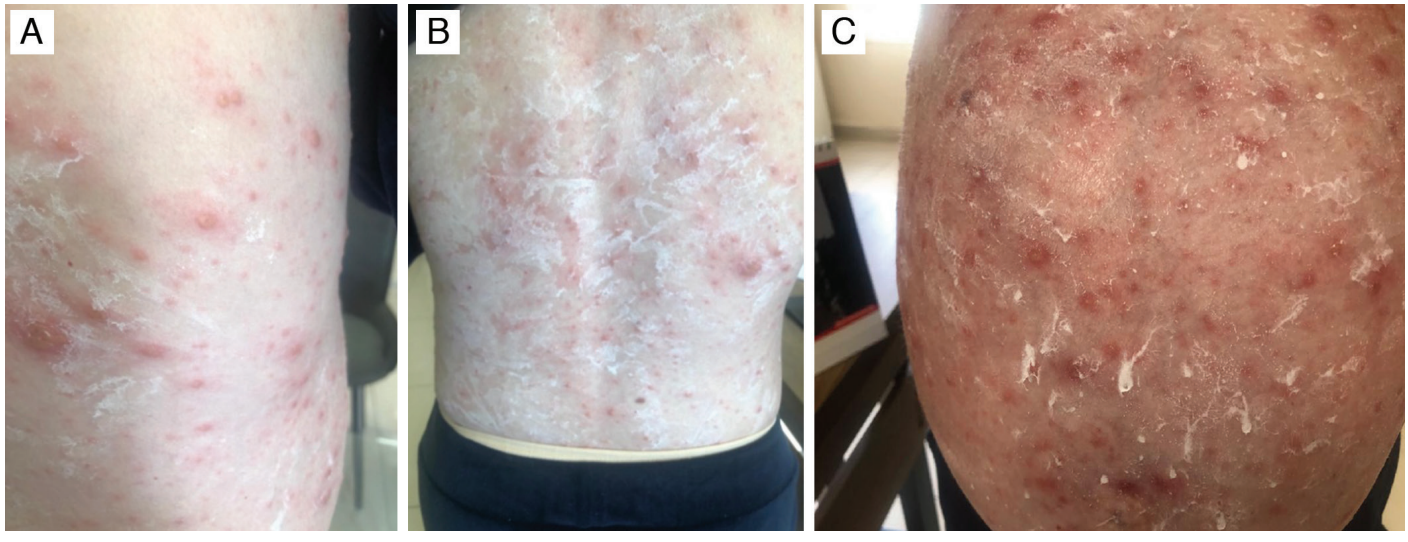

Figure 1. A, B, C) Vesicular lesions with erythematous appearance around the patient's back and abdomen

planned for the patient because the serological tests repeated twice were negative, and intravenous ampicillin-sulbactam 3x2 g/d was started due to bacterial infection secondary to itching in some lesions. Biopsy was taken from the skin lesions of the patient who was evaluated by dermatology unit. Biopsy samples taken from the lesions were evaluated by the pathology unit and interpreted as "intense mixed inflammatory cell infiltration in the epidermis with necrosis and polymorphous leukocytes in the foreground". The results of the samples sent to the Public Health Laboratory for monkeypox were negative. In the follow-up, the patient did not have high fever, the rash regressed, and the acute phase reactants decreased to the normal range. The patient was discharged with the recommendation of outpatient control.

Three weeks later, the patient was re-evaluated in the outpatient clinic, and the rash was almost completely recovered (Figure 2). VZV IgM and VZV IgG were positive in the patient whose varicella serology was studied again (Figure 3). The patient, who had more than a month after the onset of symptoms and did not have any complaints, was referred to the obstetrics and gynecology outpatient clinic after making necessary recommendations. The patient gave birth to two healthy babies.

Discussion

Chickenpox infection during pregnancy is a serious cause of mortality and morbidity for mother and fetus. It has been shown in the literature that the rate of spontaneous preterm delivery is 14.3% in pregnant women infected with chickenpox. This rate is significantly higher than the rate of 5.6% in pregnant women who are not infected with chickenpox. Fetal/newborn transmission can occur congenitally, perinatally, or postnatally[10]. Congenital chickenpox infection leads to a syndromic disease with multisystemic findings. It can cause fetal deafness, psychomotor retardation, microphthalmia, chorioretinitis, extremity hypoplasia and eschar on the skin. In the diagnosis of congenital chickenpox infection, VZV-PCR or tests that look for VZV-specific antibodies in amniotic fluid or fetal blood can be used[11]. The diagnosis of varicella infection in pregnancy is basically made clinically. Serology is often helpful in the diagnosis of chickenpox. IgM class anti-VZV antibodies usually become positive 2-3 days after the lesions appear and remain positive for 2-3 months. It is known that IgM class antibodies can also become positive again in case of reactivation. IgG class anti-VZV antibodies usually become positive 10 or more days after first contact with the virus. Therefore, serology positivity observed within the first 10 days after exposure indicates previous exposure to the virus, while serology positivity observed after the 10th day suggests the possibility of acute infection[12]. While a positive result of the VZV IgM ELISA test is typically seen in acute infection, it does not exclude reinfection and reactivation of latent VZV. Although the use of VZV IgG avidity test in cases with VZV IgG positivity gives an idea about the time of exposure to the virus, it is not routinely used in clinical practice. The sensitivity of the VZV IgM test is lower than that of showing VZV DNA from the lesion sample. The fact that the sensitivity is lower than the detection of VZV DNA in the lesion limits the routine use of the VZV IgM test. The false negativeness of the test and the inability to distinguish between reinfection/reactivation and acute infection make the use of the test problematic. However, in patients with rash, VZV IgM positivity makes the diagnosis of varicella definite[13]. Detection of VZV IgG is used to determine the immunity of a patient. Since two different samples are required to observe the increase in VZV IgG titer, its role in the diagnosis of acute disease is limited. Although VZV IgM is used in practice to support VZV active infection, it is known that the sensitivity of many commercial kits that detect IgM

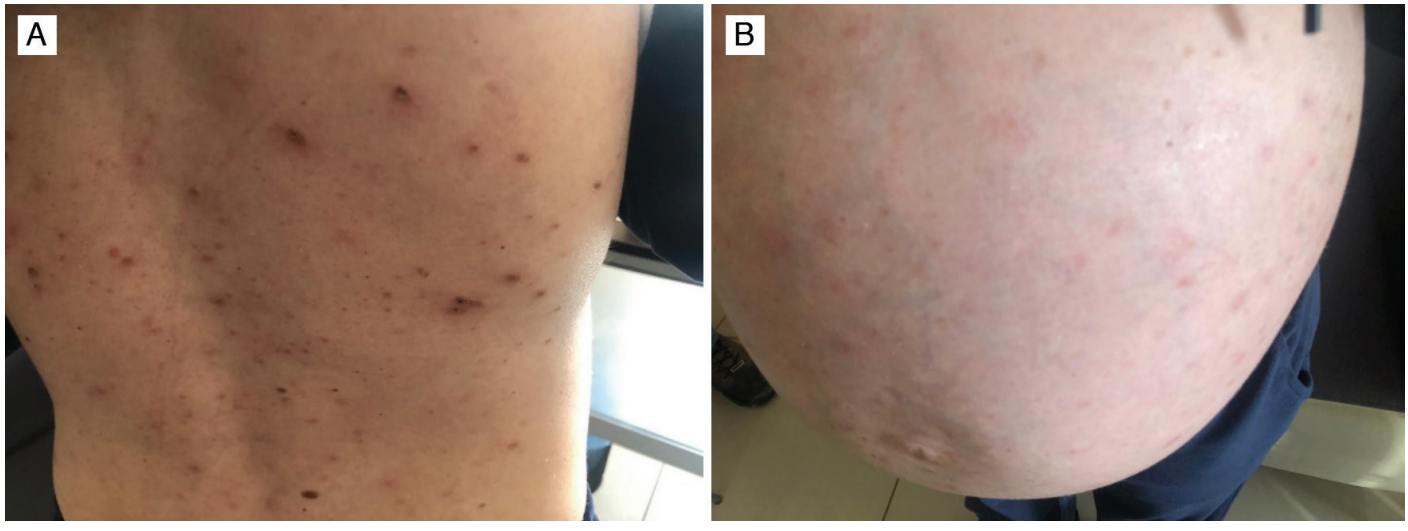

Figure 2. A, B) Final state of lesions of the patient evaluated in the outpatient clinic three weeks after discharge

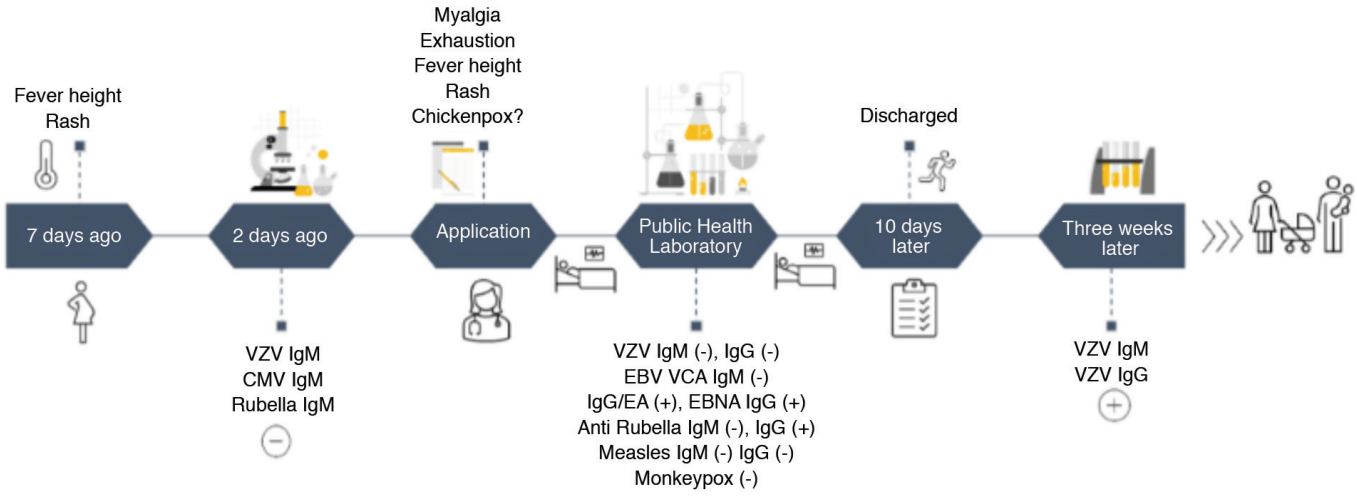

Figure 3. Timeline showing the clinical follow-up of the patient

antibodies can be variable, and false positivity can occur with other herpesviruses, especially HSV. Although the IgM antibody test of our patient was repeated more than once, the result was negative in all tests. In the literature, most of the case reports presenting pregnant women with chickenpox infection in the last trimester of pregnancy had a history of contact with an individual with chickenpox infection or IgM antibody positivity. Our patient did not state any contact history and although clinically compatible, she was found to be seronegative. In a study in which different laboratory tests used in the diagnosis of chickenpox infection were evaluated and the detection of the sample taken from the vesicles by polymerase chain reaction was defined as the gold standard, the sensitivity of antigen detection by direct fluorescent antibody test from the vesicle was 75%, the sensitivity of IgM detection in the blood was 25%, and the sensitivity of PCR in the blood was 42%[14]. In addition, prenatal diagnosis can be made by looking for VZV antibody or VZV-DNA in the amniotic fluid. It is very important to start the treatment early after the diagnosis of chickenpox infection in pregnant women. Today, antiviral therapy alone or antiviral-VZIG combination can be used in the treatment of chickenpox infection in pregnant women. Acyclovir, valacyclovir or famciclovir can be used for treatment. It has been shown that the duration of fever and other symptoms is shortened when antiviral therapy is started within the first 24 hours after the formation of the lesions[15]. There are studies showing that when antiviral treatment is started 24-72 after the formation of the lesion, it reduces the maternal mortality and morbidity associated with varicella infection. Although there are guidelines stating that it is essential to start antiviral treatment as soon as possible, there are also guidelines that do not recommend acyclovir treatment in cases where pneumonia does not develop in pregnant women, but only recommend follow-up for congenital varicella infection. Experts holding this view recommend evaluation for congenital varicella infection if varicella has developed in the first two trimesters of pregnancy, follow-up for pneumonia if it has developed in the last trimester and more than 21 days before delivery, and antiviral treatment if necessary. If VZV pneumonia develops, 10-15 mg/kg of acyclovir per day can be used in three equal doses at eight hour intervals[16]. The pregnancy category of acyclovir is known as "B". In similar case reports in the literature, VZIG was administered to pregnant women with a history of contact with individuals with chickenpox infection, and intravenous acyclovir therapy was given to pregnant women with severe clinical manifestations[17,18]. Since our patient had no history of contact, was negative for IgM antibodies and did not have pneumonia, no treatment was planned and follow-up decision was taken. Three weeks after discharge, the patient's clinical improvement and rash almost completely disappeared, and positive IgM and IgG tests confirmed the diagnosis of chickenpox infection. No pathology was found in the routine "gynecological diseases and obstetrics" visits of our patient and the two babies she gave birth to. Prevention of chickenpox infection in pregnant women is a big problem. If the pregnant woman has an active chickenpox infection four days before or two days after delivery, the newborn should be given VZIG. Considering that the occurrence of primary infection during pregnancy is the main cause of the devastating disease, the main goal for physicians is to perform VZV serology screening in all women in the reproductive period. However, the first period when VZV serology is searched in most women at this age is unfortunately the first trimester of pregnancy[19]. VZIG can be recommended to prevent severe maternal disease in pregnant

women who have a history of close contact with an individual who has recently had chickenpox infection. The conditions for recommending VZIG in various guidelines vary according to the nature and duration of contact. However, the most ideal is to administer varicella vaccine to women at this age at least 1 month before the planned pregnancy date[20].

Conclusion

Chickenpox infection during pregnancy causes severe mortality and morbidity for both mother and fetus. Women who are planning pregnancy should be evaluated for viral, bacterial and parasitic infections that may pose a risk during pregnancy. The basic approach for chickenpox should be VZV serology screening if there is no history of chickenpox infection in women in the reproductive period. If necessary, the varicella vaccine should be administered at least one month before the planned pregnancy date.

Ethics

Informed Consent: Consent form was filled out by the participant

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Ş.D., M.T., Concept: Ş.D., M.T., Design: Ş.D., M.T., Data Collection or Processing: Ş.D., M.T., Analysis or Interpretation: Ş.D., S.E., M.T., Literature Search: Ş.D., B.A., Writing: Ş.D., B.A., S.E., M.T.

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