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CASE REPORT

Congenital cytomegalovirus infection in pregnancy: a case report of fetal death in a CMV-infected woman

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Abstract
Objectives The human cytomegalovirus (CMV) is universally distributed among human populations as one of the most common cause of congenital infection with an incidence of about 0.15–2.0% in developed countries. However, controversial data concerning intrauterine fetal death caused by CMV infection exist.
Method A case report.
Results In this case report we present a stillbirth in the 18th week of pregnancy, caused by a maternal serological and fetal histological congenital CMV infection.
Conclusion Every attending physician and obstetrician should be aware of the possibility of a primary or even recurrent congenital CMV infection that could be a reason for sudden unknown congenital fetal death.

Keywords CMV · Congenital infection · Stillbirth

Introduction

The human cytomegalovirus (CMV) is universally distributed among human populations [1]. CMV is one of the most common causes of congenital infections with an incidence of about 0.15–2.0% in developed countries [2]. Severe neonatal symptoms of congenital CMV are more often in infants born to mothers with primary infection in pregnancy. Here, the typical clinical findings can be found in only about 10–15% of newborns in mothers with primary CMV infection [3, 4]. These clinical findings include intrauterine growth restriction (IUGR), microcephaly, petechiae, hepatoaplenomegalie, chorioretinitis, jaundice, cytopenia and atypical findings with a mortality rate among infants with neonatal manifestations of congenital CMV of about 10–30% [5]. Among infected infants born to mothers with recurrent infections clinical symptoms are less common. Most children with congenital CMV born to mothers with secondary CMV infection are asymptomatic at birth. Less than 10% seem to develop postnatal sequelae. Nevertheless, secondary maternal CMV may also be a significant cause of severe congenital CMV disease and in some cases may even cause intrauterine fetal death [6–10]. However, the role of CMV infection in fetal death is not fully understood. Studies by Yow et al. [11], as well as by Griffiths and Baboonian [12], reported about fetal death and spontaneous abortion in women with CMV infection. Contrast studies by Moyo et al. [13] and Eskild et al. [14] could not find a causal relationship. In this report we want to describe a case of fetal death caused by congenital CMV infection. Therefore the human cytomegalovirus should stay in the mind of every attending physician as a cause of intrauterine fetal death.

Case report

A 37-year-old gravida 3, para 2 woman in the 13th week of gestation was admitted to our hospital with the intention to treat an infection with Trichimonas vaginalis. At the time of introduction she was treated stationary in a psychiatric hospital for an acute exacerbation of a shico-affective psychosis complicated by an alcohol- and

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benzodiazepine abuse. Since no adequate medical treatment of the psychosis during pregnancy was possible (increasing rate of fetal malformation), a medical indication for an induced abortion was indicated not to endanger the live of the mother. At that time, the disorientated divorced welfare recipient without graduation released herself from hospital and could not be located until her 18th week of gestation.

However, a local therapy with clotrimazol for 6 days was started. During prenatal ultrasound care, an early intrauterine growth restriction fetus with an omphalozele was found. After passing the usual preventive medical checkup including an HIV anti-body test, TPHA test, cervix smear for Chlamydia trachomatis and usual cervix smear for bacteria (all tests without pathological findings), the patient was introduced again for prenatal diagnosis after 3 days. Surprisingly, ultrasonic verification demonstrated an intrauterine fetal death in the 18th week of gestation. An initiation to abort the pregnancy with misopsostol was started and on the same day the patient gave stillbirth to a male, growth restricted, malformated fetus of 400 g. Serologically, maternal IgM (1:160) and IgG (47.0 AE/ml) antibodies against CMV were demonstrated, indicating a primary or a recurrent CMV infection of the mother.

The histological analysis of the placenta showed a granulocitic villositis and perivillosits with detection of CMV-inclusions (Fig. 1). The autopsy of the fetus exposed a generalized cytomegalovirus infection with immunohistochemical proof of CMV-inclusions in the lungs (Fig. 2), liver, pancreas, spleen, thymus, thyroid and kidneys. Besides this, a deformity of the left arm with radiological absence of the ulna and the radius, as well as a omphalocele (1.4 × 0.8 × 0.6 cm) with exenteration of parts of the liver and the small intestine was assessed.

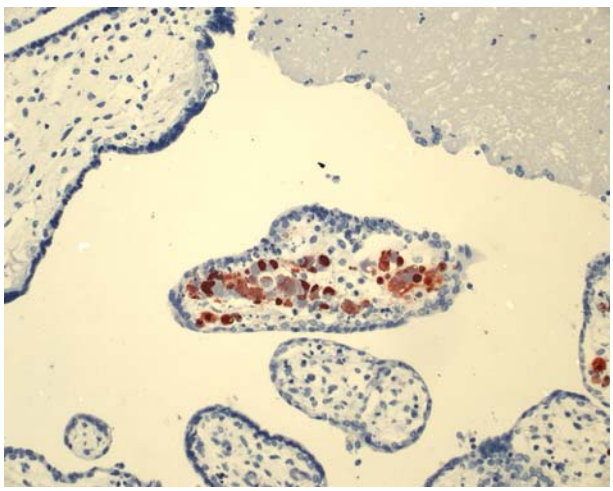

Fig. 1 CMV-placentitis with immunohistochemical proof of CMV-inclusions

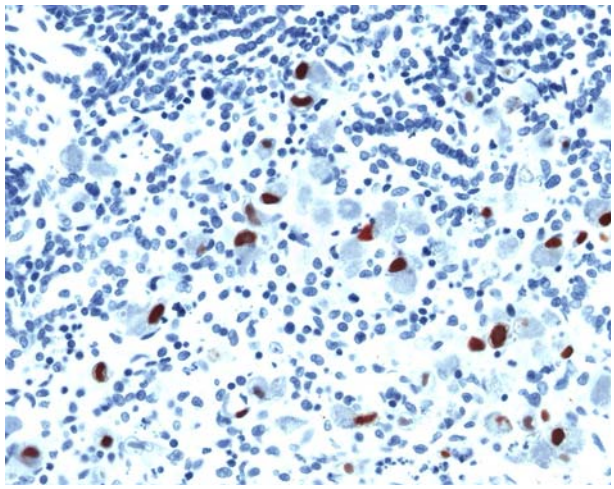

Fig. 2 Immunohistochemical reaction against CMV antibody with inclusions in the fetal lung

Discussion

Congenital cytomegalovirus infection is one of the most common intrauterine infections in pregnancy. The prevalence is higher in poor countries and in people with low socioeconomic status. In healthy individuals an initial (primary) infection is usually clinical unapparent. The virus turns into a latent state, from which it can be reactivated due to yet unknown causes, leading to a recurrent infection.

CMV can lead to congenital infections through transplacental transmission. Primary infection affects 0.7–4.1% of seronegative pregnant women and vertical transmission occurs in 20–40% of these cases [15]. Transmission of recurrent infections to the fetus ranges from 0.15–3%, depending on the population studied [1]. Although the fetus can be affected by CMV throughout the whole pregnancy, the damage is more severe in infections occurring during the first half of the pregnancy [6, 16]. The risk of symptomatic congenital CMV infection after maternal primary or secondary infection is quite unknown but it has been suggested to be as high as 15% after primary and 2% after secondary infection.

Controversial data exist concerning intrauterine fetal death caused by CMV infection. The rate of intrauterine fetal death is not known and the causes of this phenomenon are largely unknown. Yow et al. [11] reported a higher rate of spontaneous abortions and fetal death in women with primary CMV infection compared to those without an infection. In studies by Griffiths and Baboonian [12], CMV infection was seen more often in women with fetal death compared to women with life born children. Therefore, an association between maternal CMV infection and fetal death

was proposed. However, it has been postulated that these studies suffer from a limited number of cases with fetal deaths and that the estimated impact of CMV infection is uncertain [14]. Eskild et al. [14] could not find an impact of maternal CMV infection and the risk of fetal death in a study based on a source population of nearly 36,000 pregnant women. In another study by Moyo et al. [13] no increased prevalence of maternal or fetal CMV infection in over 100 cases compared to nearly 100 controls was seen.

CMV is a virus that can affect the fetal organs throughout the whole pregnancy. The damage seems to be more severe in infections occurring during the first half of the pregnancy, while infections in the second half would result in reduced morbidity [16]. Various ways of transmitting the virus to the fetus have been suggested, whereas the hematogenious spreading across the placenta with subsequent infection of placental and amniotic tissue seems to be the most common transmission way. As compared to our case report, where the histological analysis of the placenta showed a massive CMV-placentitis, Chung-Hua et al. [17] reported of a higher presence of CMV-DNA in placentas of cases with fetal death, compared to controls. The virus replicates in the oropharynx and is then carried through the fetal circulation. A large spectrum of cells in the fetus is infected by cytomegalovirus. The major target organs of CMV in the fetus are the lungs, pancreas, kidneys and the liver [3].

In our case, maternal serological data at the time of diagnosis of fetal death showed IgG and IgM antibodies against CMV, indicating a primary or a recurrent infection. Unfortunately, no earlier serum samples of the patient were available to determine the exact time point of infection. Although it is generally accepted that primary maternal CMV infection in pregnancy leads to a more severe infection of the fetus, there is increasing evidence that secondary or reactivated maternal CMV infection may also be a significant cause of severe congenital CMV disease and in some cases also cause intrauterine fetal death [5–10]. In our case, the histological analysis of the placenta showed a massive CMV-placentitis and the autopsy report of the dead fetus exposed a massive generalized cytomegalovirus infection of the fetus, including immunohistochemical proof of CMV-inclusions in the lungs, liver, pancreas, spleen, thymus, thyroid and kidneys. These findings make the congenital CMV infection as the cause of the fetal death in our case very likely.

In conclusion, every attending physician and obstetrician should be aware of the possibility of a primary or even recurrent congenital CMV infection that could be a reason for sudden unknown congenital fetal death. The best perspective would be a quick development of a safe and effective vaccine against CMV. As no vaccination is available yet, besides an education of women to prevent CMV acquisition [12], a safe and effective therapy and prevention of congenital CMV infection is still not possible. Recently, treatment of pregnant women with CMV-specific hyperimmune globuline showed very promising results in the prophylaxis of a congenital CMV infection [18]. However, this treatment option is being still under investigation.

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