

Neonatal Dengue, Case Series

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Abstract

Dengue is a viral infectious disease, it represents a problem for public health worldwide due to its morbidity and mortality. Four serotypes have been reported: DENV-1, DENV-2, DENV-3, DENV-4. Mexico is an endemic country. A series of five cases of neonatal dengue is reported from the neonatal area of the General Hospital of the West, of the Health Services of Jalisco, México, detected from February to November 2019. The importance of this report is its presentation at this age where this pathology is rare, transmission was vertical and occurred in the first days of life. The newborns had variable symptoms of the disease, one was classified as severe dengue with shock and hemorrhage. The clinical report of suspicion was confirmed with the serological diagnosis NS1/IgM (+), predominating serotype DENV-2. Vertical transmission should be suspected in high-risk areas, to maintain surveillance and once diagnosed, provide timely treatment, as well as promote the implementation of specific diagnostic and therapeutic guidelines for the neonatal stage.

Keywords: Dengue; Timely Diagnosis; Morbidity and Mortality; Neonatal Period; NS1/IgM Serology; DENV-2 Serotype

Introduction

Dengue is a viral infectious disease, it represents a problem for the Public Health worldwide due to its morbidity and mortality [1,2]. About 4 billion people live in endemic areas and it is estimated that there are about 400 million new cases each year, although only 25% are symptomatic [3].

As in Central and South American countries, in Mexico the form of transmission is through arthropods [4]. There are five epidemic arboviruses of clinical importance in humans: Dengue, Zika, West Nile Virus, Yellow Fever and Chikungunya [5]. The most clinically im-

portant types of arboviruses are the Flavivirus (a member of the family Flaviviridae) and the Alphavirus (a member of the family Togaviridae). Regarding dengue serotypes, four have been described: DENV-1, DENV-2, DENV-3 and DENV-4 (Dengue Virus serotypes 1, 2, 3, and 4) [6]. The main vectors are *Aedes aegypti* and *A. albopictus* [7] which grow in bodies of water in tropical and subtropical regions around the world. Infection with one serotype produces permanent immunity against reinfection with that serotype alone. However, a successive infection with two different serotypes is a risk factor for developing severe forms of the disease.

In 2009, the WHO developed a new classification of this disease into: severe dengue (DG) and non-severe dengue (NGD); with a third subcategory called NGD with alarm signs [8]. The main complications that arise during the dengue symptoms are derived from alterations in hemostasis, plasma leakage into the interstitial space, and organic damage, mainly liver and central nervous system [9]. The lethality of dengue when complications occur is 2 - 5% if treatment is received, but it rises to 20% when it is left untreated; while the lethality of uncomplicated cases is less than 1% [9,10].

The vertical transmission of dengue is exceptional, with an estimated prevalence of 1.6% to 10.5%. The latency period of dengue is from 3 to 25 days and more commonly from 5 to 8 days [11] it is more frequent in endemic areas and can occur when the mother is infected in the third trimester of pregnancy. The consequences of the maternal-fetal relationship have been described since the early 2000s. It has been associated with fetal losses when exposure occurs in the first weeks of pregnancy.

The clinical manifestations are well described, but many still do not have clear pathophysiological mechanisms [12]. The appearance of signs and symptoms in the newborn has been described, which can present from nine hours postpartum to 11 days of extrauterine life, with the mean being 3.4 days [13-17] is characterized by fever, morbilliform skin rash, and hepatomegaly. In the laboratories we can find thrombocytopenia, leukopenia and an increase in transaminases 5 to 10 times above their normal range. Although the real impact on the health of the maternal-fetal binomial is still not well clarified, we know that morbidity and mortality increases by up to 25% in these cases and the severity of the clinical presentation is directly associated with the level of involvement of the binomial in the short and medium term [18-20].

In newborns, dengue infection may be due to a vertical infection, the maternal history being important and in the face of clinical suspicion, establish the diagnosis with the detection of NS1 in serum from day 0 to 5 days after the start of the symptoms and IgM after this period [21].

That is why it is important in the face of a compatible clinical picture in the mother, and once confirmed, to continue with the diagnosis of the newborn.

Clinical Cases

A series of 5 cases of neonatal dengue from the neonatology area of the Hospital General de Occidente, of the Jalisco Health Services, detected from February to November 2019, is reported (Table 1).

Discussion

In 2019, there was an increase in the incidence of dengue at a global level. In Mexico, 41,505 cases were reported, with Jalisco being the state with the highest reported cases, up to 69%, followed by Veracruz, Chiapas, Quintana Roo, and Oaxaca [22,23]. Factors such as global warming, deficient water treatment, as well as population growth, migration and human movements have increased the risk of its transmission.

Within our hospital unit, the diagnosis was obtained in 5 newborns confirming vertical transmission, only in one of them the serotype was not identified because the study was carried out in a private environment. The clinical evolution in the 5 cases was similar to that

Case	1	2	3	4	5
Gender/Gestational age	Male 34.2 weeks	Female 33.2 weeks	Female 34 weeks	Male 33.2 weeks	Male 33.2 weeks
Days of onset of maternal fever before birth	3 days	7 days	3 days	2 days	5 days
Evolution	4 th day of life, hypoactive, jaundice, thrombocytopenia, PCR 0.35 mg/dl, procalcitonin 0.78	4 th day of life jaundice, apnea, oral rejection, thrombocytopenia, PCR 0.56 mg/dL, Procalcitonin 0.33	5 th day of life, apnea, fever, hypoactivity, petechiae, upper gastrointestinal bleeding, leukopenia, thrombocytopenia, hyponatremia, PCR 0.22 mg/dL, procalcitonin 2.41	7 th day of life, fever, hypoactivity, leukopenia, thrombocytopenia, PCR 0.5 mg/dL Procalcitonin 0.24	2 nd day of life, oral intolerance, jaundice, thrombocytopenia, PCR 0.42 mg/dL Procalcitonin 0.13
Maternal PCR	DEN-V (+)	DENV-2 (+)	DENV-2 (+)	DENV-2 (+)	DENV-2 (+)
Newborn PCR	(-)	DENV-2 (+)	DENV-2 (+)	DENV-2 (+)	DENV-2 (+)
Newborn serology (NS1/ IGM)	(+)	(+)	(+)	(+)	(+)
Blood culture	Negative	Negative	Negative	Negative	Negative
Resolution	Hospital discharge	Hospital discharge	Death	Hospital discharge	Hospital discharge

Table 1: Clinical data and evolution of the cases.

described in patients with early and late neonatal sepsis, which makes their diagnosis by exclusion and suspicion of a history of maternal infection, being diagnosed within the first 7 days of life.

In 2007 Fernandes [24] reports 7 cases in Brazil, the diagnosis was by antibodies, PCR in maternal or newborn serum and analysis of ovular and placental remains. They found that the time for the onset of symptoms in the newborn was between 1 and 8 days on average; 2 of these cases were completely asymptomatic. The reason for admission was respiratory distress, leukopenia represented the most common finding, 1 was abortion, and 1 mother died. Xueru Yin [25] reports a case of vertical transmission in a 25-year-old patient and 39 weeks pregnant. A term newborn with good birth weight with thrombocytopenia up to 29,000 Xmm³ and leukopenia up to 1.3% Xiong, *et al.* [26] in a meta-analysis found that eleven studies report the impact of dengue on pregnancy and low birth weight. 8 studies in Latin America and 3 in Asia, in which they did not find solid evidence that the infection increases the risk of prematurity, weight under abortion or death. J. Alallah, *et al.* [27] report a patient diagnosed with dengue during the 13th week of pregnancy whose follow-up at 29 weeks presented severe microcephaly and reminds us that although the association of microcephaly is not as frequent as in Zika there is evidence of the manifestations above all Neurological disorders in the children of mothers with symptomatic dengue infections in early stages of pregnancy. In the analysis of our patients, 4 were premature and only one at term. A report of Haryanto [28] in a mother who was admitted with dengue symptoms, the neonate presented clinical data of severity 3 days after the cesarean section: the diagnosis in

the neonate which at the beginning with a negative antigen test, subsequently presented thrombocytopenia and fever being the sixth day, ELISA positive. Emphasizing that, although sensitive and specific, antigen tests must be corroborated when there is clinical suspicion. Of the reported cases, most of the symptomatic patients were treated with broad and very broad spectrum antibiotics, however, there were no isolates in the microbiological studies taken.

In Mexico, various publications have been made with case reports and case series, one of them in 2015 by Romero Santacruz, *et al.* where 7 cases are described in neonates between 34 and 40 weeks of gestation with a history of maternal infection with positive IgM serology diagnoses, like our cases, with the presence of thrombocytopenia and in one of them with shock and hemorrhage [29]. Arredondo García, *et al.* document that in 2019 the most frequent serotypes found were DEN-1 and DEN-2; in our series, 4 were reported for DEN-2 [30].

Conclusion

In our environment, dengue continues to be a public health problem. Clinical suspicion in newborns with a history of symptomatic mothers in the last two weeks of pregnancy should prevail, especially in high-risk areas. By having reports of vertical transmission, they must be established in the same way with diagnostic and management guidelines for patients in the neonatal stage, which is a proposal with solid bases.

Prevention in the spread of the mosquito continues to be one of the basic pillars for the reduction of cases, information in the mass media and even within schools is an important primary strategy. The evidence so far shows us that the most important actions continue to be covering clean water containers with lids (using or not insecticides) and the controlled collection of garbage in homes.

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Conflict of Interest

None.

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