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CLINICAL CASE

Dengue with unusual clinical features in an infant. Case report

Dengue, presentación inusual en un lactante. Reporte de un caso

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Abstract

Introduction: The state of Yucatan, in Mexico, is an endemic area for dengue. During 2015, there was an unexpected increase in the number dengue fever cases. **Objective:** To describe and analyse the clinical presentation, progress, and management of a case of dengue infection with non-specific clinical manifestations in an infant, associated to a dengue shock syndrome. **Case report:** One month-old infant admitted to hospital with a generalised rash and a history of being bitten by an insect. Anaphylaxis was diagnosed based on clinical manifestations and anamnesis. The infant developed hypotension, tachycardia, anaemia, and respiratory distress. He was transferred to the intensive care unit, dying on the fifth day. He tested positive to dengue virus in the PCR test and for IgG antibodies using Elisa. The cause of death was a dengue shock syndrome. **Conclusions:** Dengue fever in young infants may be afebrile, so it is important to suspect them appropriately in the presence of a generalised rash, tachycardia, and hypotension, in order to avoid the deadly consequences of dengue shock.

Keywords:
Dengue shock syndrome;
Dengue;
Infant;
Anaphylaxis;
Mexico

Introduction

During the year 2015, in Mexico there was an increase in the number of dengue cases in 76% for probable cases and 19% in confirmed cases. The state of Yucatan ranked fourth in incidence at the national level, with circulation of serotypes 1, 2 and 4. By the epidemiological week 52, 3 lethal cases of dengue had been confirmed in Yucatan, among which is the one that here we present[1]. The objective was to describe and analyze the clinical presentation of a case of dengue infection with nonspecific clinical manifestations in a minor infant, which resulted in dengue shock syndrome, its evolution and in-hospital management.

Clinical case

One-month-old male infant, single term product of the second gestation of a couple living in an urban setting in Yucatan (Mexico). Son of a 19-year-old mother with secondary schooling and 20-year-old father with incomplete preparatory schooling. At birth the infant weighed 3535 g, height 50 cm, the newborn was at-

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tended at the hospital, obtained by vaginal route and discharged with the mother at 24 h of birth. The only antecedent of relevance during gestation was 2 infections of the urinary tract, one in the 5th and the other in the 8th month, successfully treated. He lived with 7β people in a 2βroom dwelling with basic urbanization and hygiene services, without mosquito nets on doors and windows. The patient showed normal somatic and psychomotor development and was fed to the maternal breast supplemented with formula.

After 33 days of extrauterine, life he was taken to the emergency room due to the bite of one or more insects (unspecified) associated with the formation of 2βerythematous papules on the medial side of the left lower limb, which were not painful on palpation. In addition, the infant had irritability, crying, rejection of the oral route and vomiting on one occasion. In his vital signs, attention was drawn to the presence of tachycardia of 188 beats per minute, but other additional alterations were identified. It was diagnosed as an allergic secondary reaction to insect bite, so he received antihistamine-based management. Hours after his hospital admission, the patient developed a generalized erythema that yielded to the digitopression. Anemia data (Hb: 10,7βg/dL) were found in the laboratory results, with a slight decrease in hematocrit. Likewise, it presented hypoalbuminemia (2,6βg/dL), delayed coagulation times with mild hypocalcemia and additionally elevated phosphate, magnesium and glucose was observed. The other values, including the values of the white formula, were within the ranges of normality (table 1).

Table 1. Laboratory test results during hospital stay

Test	Day 1	Day 2	Day 3	Day 3 bis	Day 5	Day 6	Conventional unit	Normal values
Total proteins	3.8	5.3	-	-	-	-	g/dL	6.6-8.7
Albumin	2.7	3.2	2.6	-	4	3.2	g/dL	3.8-5.1
TBT	0.9	0.6	0.5	-	0.5	0.5	mg/dL	1.2
UB	0.6	0.2	0.3	-	0.3	0.2	mg/dL	0-0.25
CB	0.3	0.4	0.2	-	0.2	0.3	mg/dL	0-0.75
AST	92	249	244	-	144	131	U/l	0-31
ALT	-	27	44	-	36	33	U/l	0-32
AP	331	364	355	-	262	222	U/l	64-306
LDH	362	-	-	-	-	2.682	U/l	225-450
PT	21.7	-	14.70	-	-	-	s	11.5-15.3
PTT	69.6	-	51.6	-	-	-	s	35.1-46.3
INR	-	-	1.22	-	-	-		0.86-1.22
Ca	8.4	8.1	7.9	9.7	8.5	11.8	mmol/l	8.9-10.3
Na	135	136	123	136	140	126	mmol/l	136-144
Cl	108	103	97	101	109	102	mmol/l	101-111
K	4	4.9	5.2	4.6	5.8	4.8	mmol/l	3.6-5.1
P	6.8	-	4.6	4.2	5.2	4.8	mmol/l	2.4-4.7
Mg	2.73	-	2.25	2.41	2.1	2.33	mmol/l	1.8-2.5
Leukocytes	9.800	11.500	23.100	-	26.900	34.400	× 10^3/Ul	4.000-19.500
Neutrophils (%)	58.9	89.5	72.8	-	84.4	78.1	× 10^3/Ul	1.4-6.5
lymphocyte. (%)	35.60	9.1	20.5	-	6.7	10.4	× 10^3/Ul	1.2-3.4
Eosinófilos (%)	0.3	0.1	0.1	-	0.1	0.1	x 10^3/Ul	0-0.4
Hemoglobin	10.7	12.6	12.8	-	9.8	11.1	g/dL	10.7-13.9
Hematocrito	31.4	39.1	37.8	-	28.9	34.7	%	33-44
Platelets	321.000	208.000	110.000	-	11.000	10.000	× 10^3/Ul	150-350
ESR	14	-	-	-	1	-	mm/h	15
PCR	0.34	2.97	3.88	1.73	2.44	1.95	mg/dL	0.75
Glucosa	305	171	110	216	179	1.018	mg/dL	75-110
Urea	17.1	57.8	-	40.7	59.9	57.8	mg/dL	10-50
Creatinine	0.5	0.6	0.5	0.5	0.9	1.1	mg/100 mL	0.2-0.4
UN	8	27	25	19	28	27	mg/dL	7-18

ALT: alanine aminotransferase; AST: Aspartate aminotransferase; TB: Total bilirrubines; UB: Unconjugated bilirubin; CB: conjugated bilirubin; UN: Urea nitrogen; LDH: Lactate dehydrogenase; AP: alkaline phosphatase; INR: international normalized ratio; PCR: polymerase chain reaction; PT: Prothrombin time; TTP: Partial thromboplastin time; VSG: erythrocyte sedimentation rate.

On the second day of evolution, a delayed capillary filling, tachycardia of 200 beats per minute, distal cyanosis, and expiratory difficulty were identified in the infant, through which support was initiated with oxygen therapy and management based on crystalloid solutions, adrenaline, Hydrocortisone, diphenhydramine and atropine. The patient continued with desaturation and respiratory failure, so that endotracheal intubation was performed in AC mode with high parameters: saturation was achieved at 100%, sedation based on fentanyl was initiated and a subclavian catheter was placed. New laboratories including polymerase chain reaction (PCR), serology for dengue and blood culture were taken.

On the third day of hospital stay, he was transferred to the Pediatric Intensive Care Unit (PICU). From his admission to the PICU he required high ventilatory values and, although these values increased during his stay in the PICU, the patient persisted with hypoxemia data. Hours after the onset of ventilation, the patient presented left pneumothorax, which was treated with the placement of pleural seal, without further eventualities. Subsequently, the infant had a supraventricular tachycardia that was managed with adenosine, amiodarone and lidocaine, which reversed the arrhythmia. Given the current shock data, it was treated with vasoactive drugs and milrinone, without achieving its stabilization. In the general examination of urine, the presence of discrete proteinuria was observed.

Control laboratories were requested on the fourth day, including blood chemistry, blood biometry and coagulation times. Among the results, leukocytosis (23,100 / mL) was found at the expense of neutrophilia, as well as thrombocytopenia (110,000 / mL). The numbers of thrombocytes were decreased according to a subsequent platelet count control (110,000 to 11,000 / mL) and, within a few hours, the presence of hepatomegaly 2β cm below the costal ridge and the total absence of peristalsis appeared in his clinical picture.

During the fifth and sixth days, the infant continued under sedation and evolved with generalized hypoperfusion, severe edema in extremities, distal necrosis and marked cyanosis. On the seventh day, oxygen saturation decreased to 30% and was followed by cardiorespiratory arrest, which led to advanced resuscitation maneuvers, with no response. Subsequent to death, the result was received by PCR and capture IgG, both positive for dengue. The diagnoses of death were shock syndrome due to dengue, sepsis and left pneumothorax.

Discussion

This report presents a case of dengue shock syndrome, which during the first hours of evolution and its arrival in the hospital was afebrile, and whose clinical condition was characterized by generalized erythema, tachycardia, hypotension and, subsequently, respiratory distress, which was diagnosed and treated as a case of anaphylactic reaction. Clinical manifestations of anaphylactic reactions in infants (≤2 years) tend to be afebrile with angioedema and generalized erythema accompanied by tachycardia and hypotension. If we add to this the history of an insect that is not specified, the clinical picture was considered suggestive of anaphylaxis. Simmons et al. mention that the standardized test of tryptase in mastoid cells is the one of choice for the diagnosis. However, there is no such test in the place of care. The values of basophils tend to increase in the cases of anaphylaxis, which did not happen in the case presented here[2,3].

The patient developed respiratory distress and required mechanical ventilation, which could be the cause of the pneumothorax he developed thereafter. The presence of pneumothorax after mechanical ventilation has been previously described in younger infants[4].

The chronological evolution of the events in the infant showed a phase of viremia verified by PRC in which he attended afebrile during his stay in hospital, but in which he already showed delay in coagulation times, accompanied by hypotension followed by a phase of extravasation of fluid to third space with thrombocytopenia and altered liver function and blood pressure, which led to dengue shock syndrome. Previously, the afebrile presentation of dengue infection in infants has been reported, accompanied by generalized erythema, as manifested in the infant of the present case[5].

The immunological importance of antibodies is its defense function in the prevention and control of many infections. Virus specific antibodies act by neutralizing the virus and thus by preventing infection, either by cell lysis, by activating the complement cascade or by binding to the receptors of the defense cells. However, there is also a phenomenon known as antibody amplification (ADA) whereby antibodies can increase or amplify viral replication. The ADA has been described for the case of dengue infections[6].

Dengue ADA is associated with the severity of clinical manifestations in neonates and minor infants, which is directly dependent on the mother's antigenic memory. Because infectivity-dependent antibody stimulation is central to pathogenesis, newborns of dengue immune mothers, when maternal antibodies decline, enter a "window period" characterized by declining levels of antibodies. These levels of antibodies, although on the decline, may still be sufficient to increase the infant's response, leading to the production of inflammatory, vasodilatory molecules that promote vascular permeability and facilitate dengue shock syndrome. The positive result for RPC in the infant in-

dicates the presence of the virus and the titers above the cutoff point in the IgG capture antibody values reported by the official epidemiological reference laboratory indicate that the infant had antibody titres corresponding to a secondary infection, which could happen because, in addition to studying the active dengue infection, he also had maternal antibodies. Dengue *shock* occurs in young children and is preceded by persistent hypotension and hypoxia that, if unresolved, trigger death[6–11].

During the epidemiological period in which this case occurred, an outbreak of chikungunya, a virus that was not ruled out in the infant, was also present, as were other bacterial diseases prevalent in the region[12].

The sociodemographic characteristics such as living in overcrowding, in the presence of vectors and being the child of an adolescent mother, coupled with the nutritional aspects derived from being fed with formula at such a young age could be factors that facilitated transmission and infection.

Ethical Responsibilities

Human Beings and animals protection: Disclosure the authors state that the procedures were followed according to the Declaration of Helsinki and the World Medical Association regarding human experimentation developed for the medical community.

Data confidentiality: The authors state that they have followed the protocols of their Center and Local regulations on the publication of patient data.

Rights to privacy and informed consent: The authors have obtained the informed consent of the patients and/or subjects referred to in the article. This document is in the possession of the correspondence author.

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Conflicts of Interest

Authors state that any conflict of interest exists regards the present study.

References

1. SINAVE/DGE/SSA. Información y Vigilancia Epidemiológica de Dengue. Sistema de Vigilancia Epidemiológica de Dengue/ Información a 4 de enero de 2016. En: Epidemiología. DGd, editor. México; 2016.
2. Simons FER, Sampson HA, Anaphylaxis. Unique aspects of clinical diagnosis and management in infants (birth to age 2 years). J Allergy Clin Immunol. 2014;135:1125-31, http://dx.doi.org/10.1016/j.jaci.2014.09.014
3. Golden DB. New directions in diagnostic evaluation of insect allergy. Curr Opin Allergy Clin Immunol. 2014;14:334-9.
4. Bhat Yellanthoor R, Ramdas V. Frequency and intensive care related risk factors of pneumothorax in ventilated neonates. Pulm Med. 2014;2014.
5. Aurpibul L, Khumlue P, Oberdorfer P. Dengue shock syndrome in an infant. BMJ Case Rep. 2014;2014, bcr2014205621.
6. Parameswaran P, Liu Y, Roskin KM, et al. Convergent antibody signatures in human dengue. Cell Host Microbe. 2013;13:691-700.
7. Peyerl-Hoffmann G, Schwöbel B, Jordan S, et al. Serological investigation of the prevalence of anti-dengue IgM and IgG antibodies in Attapeu Province, South Laos. Clin Microbiol Infect. 2004;10:181-4, http://dx.doi.org/10.1111/j.1198-743x.2003.00854.x
8. Halstead SB. Antibody, macrophages, dengue virus infection, shock, and hemorrhage: A pathogenetic cascade. Rev Infect Dis. 1989;11 Supplement 4:S830-9.
9. Kliks SC, Nimmanitya S, Nisalak A, Burke DS. Evidence that maternal dengue antibodies are important in the development of dengue hemorrhagic fever in infants. Am J Trop Med Hyg. 1988;38:411-9.
10. Simmons CP, Chau TN, Thuy TT, et al. Maternal antibody and viral factors in the pathogenesis of dengue virus in infants. J Infect Dis. 2007;196:416-24, http://dx.doi.org/10.1086/519170
11. Halstead SB. Dengue. Lancet. 2007;370:1644-52.
12. Méndez N, Ojeda-Baranda R, Baeza-Herrera L, Gómez-Carro S. Perfil clínico-epidemiológico de los casos de Chikungunya atendidos en el Hospital Agustín O´Horán en 2015. PAHO. 2016. Under review.