医薬品 研究報告 調査報告

識別番号・報告回数			報告日	第一報入手日	新医薬品等の区分	機構処理欄
				2007. 9. 20	該当なし	

一般的名称	解凍人赤血球濃厚液	研究報告の公表状況	Ramful D, Carbonnier M, Pasquet M, Bouhmani B, Ghazouani J, Noormahomed T, Beullier G, Attali T, Samperiz S, Fourmaintraux A, Alessandri JL. Pediatr Infect Dis J. 2007 Sep;26(9):811-5.	公表国 フランス
販売名(企業名)	解凍赤血球濃厚液「日赤」(日本赤十字社) 照射解凍赤血球濃厚液「日赤」(日本赤十字社) 解凍赤血球-LR「日赤」(日本赤十字社) 照射解凍赤血球-LR「日赤」(日本赤十字社)			

研究報告の概要

○チクングニヤウイルス感染症の母子伝播

背景:2005年～2006年に仏領レユニオン諸島でチクングニヤ熱(蚊媒介性アルファウイルス感染)のアウトブレイクが起こった。この流行期間中、母子伝播の可能性が高い早期新生児症例が認められた。

方法:5つの新生児医療部門において後方視的記述的研究を実施した。チクングニヤウイルス感染は、RT-PCR法又は母親と新生児の特異的血清検査にて確認した。出産時に徴候があった場合又は新生児が出生初日に発病した場合に母親のスクリーニングを行った。

結果:新生児38名を登録した。無症候の母親2名を除き、全母親に周産期[範囲:分娩前4日～分娩後1日]の症状が存在した。新生児にはいずれも症状があり、症状は出生後3日～7日(平均4日)に発現した。母体の疾患発症から新生児の疾患発症までの平均期間は、5日間(範囲3～9日間)であった。新生児にもっとも多く見られた臨床徴候は、発熱(79%)、疼痛(100%)、発疹(82%)、末梢浮腫(58%)であった。血小板減少症(76%)、リンパ球減少症(47%)、プロトロンビン低下(65%)、AST上昇(77%)が検知された。合併症には、発作(6)、出血性症候群(6)、血行動態障害(10)が認められた。脳髄液のRT-PCR法は24名中22名で陽性であり、25名中14名に脳MRIの異常所見(白質の病変または実質内出血、あるいはその両方)が認められた。心エコー検査では、心筋肥大(5)、心室機能不全(2)、心膜炎(2)、冠動脈拡張(6)が示された。新生児1名は壊死性腸炎で死亡した。

結論:レユニオン諸島で発生したチクングニヤ熱流行により、周産期母子伝播の罹患率が高い可能性が初めて明らかとなった。

使用上の注意記載状況・その他参考事項等

解凍赤血球濃厚液「日赤」
照射解凍赤血球濃厚液「日赤」
解凍赤血球-LR「日赤」
照射解凍赤血球-LR「日赤」

血液を介するウイルス、細菌、原虫等の感染
vCJD等の伝播のリスク

報告企業の意見	今後の対応
2005年～2006年に仏領レユニオン諸島で発生したチクングニヤ熱の大規模流行期間中、母子伝播の可能性が高い早期新生児症例が認められたとの報告である。	日本赤十字社では、輸血感染症対策として問診時に海外渡航歴の有無を確認し、帰国後4週間は献血不適としている。国内でチクングニヤ熱が確認されたため、渡航歴確認の徹底を図っている。また、チクングニヤ熱の既往歴がある場合、治癒後6ヵ月間は献血不適としている。今後も引き続き、新興・再興感染症の発生状況等に関する情報の収集に努める。

(19)

Mother-to-Child Transmission of Chikungunya Virus Infection

Duksha Ramful, MD, Magali Carbonnier, MD,† Marlène Pasquet, MD,* Brahim Bouhmani, MD,† Jamal Ghazouani, MD,‡ Tahir Noormahomed, MD,§ Gilles Beullier, MD,‖ Tania Attali, MD,* Sylvain Samperiz, MD,* Alain Fourmaintraux, MD,† and Jean-Luc Alessandri, MD**

Background: In 2005–2006 Reunion Island experienced a massive outbreak of chikungunya, a mosquito-borne alphavirus infection. During this epidemic, early neonatal cases were observed with a highly probable mother-to-child transmission.

Methods: A retrospective descriptive study was conducted in 5 neonatal medicine departments. Chikungunya virus infection was confirmed by reverse transcription-polymerase chain reaction or specific serology in mothers and their newborns. Mothers were screened if they presented signs at delivery or if their neonates became ill on the first days of life.

Results: Thirty-eight neonates were enrolled. All mothers, except 2 asymptomatic mothers, presented signs during the perinatal period (range, day(D) −4 to D+1). All neonates were symptomatic and presented symptoms on D3 to D7 (mean, D4). The mean interval between onset of maternal illness and onset of neonatal illness was 5 days (range, 3–9). The most frequent clinical signs in neonates were fever (79%), pain (100%), rash (82%), and peripheral edema (58%). Thrombocytopenia (76%), lymphopenia (47%), decreased prothrombin value (65%), and elevation of aspartate aminotransferase (77%) were detected. Complications included seizures (6), hemorrhagic syndrome (6), and hemodynamic disorders (10). Reverse transcription-polymerase chain reaction in cerebrospinal fluid was positive in 22 of 24 cases, and abnormal findings on brain magnetic resonance imaging (14 of 25) with white matter lesions or intraparenchymal hemorrhages or both were found. Echocardiography (16) showed myocardial hypertrophy (5), ventricular dysfunction (2), pericarditis (2), and coronary artery dilatation (6). One neonate died of necrotizing enterocolitis.

Conclusions: The chikungunya epidemic that occurred on La Reunion Island revealed for the first time the possibility of mother-to-child transmission in the perinatal period with a high rate of morbidity.

Accepted for publication March 22, 2007.

From the *Service de Réanimation Néonatale et Pédiatrique, CHD Félix Guyon, Saint-Denis de La Réunion; †Service de Réanimation Néonatale et Pédiatrique, Groupe Hospitalier Sud Réunion; ‡Service de Pédiatrie, Centre Hospitalier Intercommunal Saint-Benoit; §Service de Néonatologie, Clinique Sainte-Clotilde; and ‖Service de Pédiatrie, Centre Hospitalier Gabriel Martin, La Réunion, France.

Address for correspondence: Duksha Ramful, MD, Service de Réanimation Néonatale et Pédiatrique, Centre Hospitalier Départemental Félix Guyon, 97405 Saint-Denis Cedex, La Réunion, France. E-mail: duk@gawab.com.

ISSN: 0891-3668/07/2609-0811
DOI: 10.1097/INF.0b013e3180616d4f

Key Words: chikungunya, alphavirus, neonate, pregnancy, mother-to-child transmission
(*Pediatr Infect Dis J* 2007;26: 811–815)

The islands of the southwest Indian ocean, including La Reunion Island (east of Madagascar), have been exposed since 2005 to an epidemic of chikungunya, an arbovirus infection transmitted by a mosquito of the *Aedes* genus (*Aedes albopictus* in La Reunion Island).[1] The chikungunya virus (CHIKV) is an alphavirus of the Togaviridae family,[2] isolated for the first time in Tanzania and Uganda in 1953.[3,4] It has developed according to an endemic or epidemic mode in sub-Saharan Africa, Southern India, Southeast Asia, and in the Pacific.[5–8] CHIKV is a single-chain linear RNA virus with a diameter of 60–70 nm, enclosed by an envelope.[2]

Clinical signs and symptoms of chikungunya in adults and children are preceded by an incubation period of 4–7 days. CHIKV infection usually presents with sudden onset of high fever and disabling joint and muscle pain (chikungunya is a Swahili word meaning "that which bends up," referring to the stooped walk of patients), often associated with a maculopapular rash and gastrointestinal complaints.[9,10] A hemorrhagic syndrome, generally minor, has also been described, consisting of petechial purpura, epistaxis, or bleeding gums.[11] The natural history of the disease is usually favorable with complete resolution within 1 week. Chronic forms are possible with persistence or recurrence of arthralgia for several months. Complications reported in adults and children are neurologic (meningoencephalitis, polyneuropathy), hemorrhagic,[12–17] and cardiac (pericarditis, myocarditis, cardiac arrhythmias).[18–21] No case of mother-to-child transmission was described before the La Reunion Island epidemic. The youngest child infected by CHIKV reported in the literature before this epidemic was a 21-day-old infant.[15]

The laboratory diagnosis of CHIKV infection is based on 2 types of tests: detection of viral RNA by reverse transcription-polymerase chain reaction (RT-PCR) and IgM- and IgG-specific serology. RT-PCR is positive during the viremic phase lasting for 1 week after onset of symptoms. Specific IgM antibodies are detected by the fifth day after onset of the disease and persist for several weeks to 3 months, whereas specific IgG appear on the 15th day and persist for years.[1]

The first case of chikungunya in La Reunion Island was reported in March 2005. The epidemic was surprising in terms of its magnitude and the development of clinical forms

that had rarely or never been previously described. The epidemic peak was reached between January 2006 and February 2006 with 46,000 cases per week during this period.[1] At the end of April 2006, the estimated cumulative number of cases was 256,000, ie, 33% of the La Reunion Island population. We report a series of 38 neonates with CHIKV infection during the first week of life after perinatal mother-to-child transmission of the virus. Some cases have already been reported in a previous publication.[22]

PATIENTS AND METHODS

This is a retrospective descriptive study conducted by 5 neonatal medicine departments in public or private hospitals complying with European standards with air-conditioned mosquito-free maternity units. Thirty-eight neonates born between March 2005 and April 2006 were included in this study. Charts were reviewed by 2 investigators.

Definition. The diagnosis of neonatal CHIKV infection was based on RT-PCR detection of the viral genome in the neonate's serum or cerebrospinal fluid (CSF) or both during the first week of life and/or detection of serum anti-CHIKV IgM during the first 15 days of life. The diagnosis of maternal CHIKV infection was based on RT-PCR detection of the viral genome in serum or the presence of serum anti-CHIKV IgM or both. Mothers were screened if they presented signs of chikungunya at delivery or if their neonates became ill on the first days of life. Mother-to-child transmission of CHIKV infection was diagnosed when CHIKV infection was diagnosed in the mother during the perinatal period and when CHIKV infection was diagnosed in her newborn infant during the days after birth, according to the criteria defined above.

Laboratory Methods. Detection of serum anti-CHIKV IgM was performed by an immunocapture method (Mac-ELISA) according to the techniques and reagents of the Centre National de Référence des Arboviruses (National Reference Centre) in Lyon and the Centre National de Référence of the Institut de Médecine Tropicale du Service de Santé des Armées (Armed Forces Institute of Tropical Medicine) in Marseille: capture of IgM by a serum antihuman IgM (I-2386; Sigma, St. Louis, MO), successive addition of CHIKV antigen prepared in cell culture, followed by hyperimmune murine ascites, and revelation of the antibody by peroxidase-marked antimouse conjugate (Sigma, A-0168).

RT-PCR detection of the viral genome was performed after extraction in 200 μL of sample either manually using Viral QIAAmp Minikit (Qiagen, Courtaboeuf, France) or on the MagNa Pur automat (Roche Diagnostic) using the High Pure Viral RNA kit (Roche Diagnostic). RT-PCR was performed with the SuperScript One-Step RT-PCR with Platinium *Taq* kit according to the method of Pastorino et al.[23]

Maternal Data and Outcome of Pregnancies. The following data were recorded: date of onset of symptoms of CHIKV in relation to delivery, fetal heart rate abnormalities, mode of delivery, and birth term.

Neonatal Clinical Data and Complementary Investigations. The following clinical data were analyzed: birth weight, sex, age of onset of signs of illness, type of signs, any complications, and short-term course. Pain was assessed using the EDIN (Echelle Douleur Inconfort Nouveau-Né, neonatal pain and discomfort scale). The following treatments were recorded: analgesia, red blood cell or platelet transfusions, and fresh frozen plasma. Laboratory data recorded, whenever possible, were complete blood count and platelets, serum calcium, hepatic and cardiac enzymes, hemostasis, C-reactive protein, and CSF analysis. Results of the following complementary investigations were analyzed: head ultrasound and brain magnetic resonance imaging (MRI). The MRI protocol comprised T1, T2, and diffusion sequences. In one of the centers, a cardiologic assessment was systematically performed in 16 neonates, comprising laboratory work-up [aspartate aminotransferase, creatine protein kinase, creatine kinase myocardial fraction, and troponin Ic], electrocardiogram, and transthoracic echocardiography.

RESULTS

Diagnosis of CHIKV Infection for Mother-Child Pairs. Thirty-eight neonates presented documented mother-to-child transmission of CHIKV infection. The diagnosis of maternal infection was confirmed by RT-PCR detection of CHIKV (21 of the 26 mothers tested) or by the presence of specific anti-CHIKV IgM (21 of the 24 mothers tested) or both. The diagnosis of neonatal infection was confirmed by RT-PCR (24 of the 24 neonates tested) or by the presence of specific IgM (26 of the 30 neonates tested) or both.

Maternal History. Thirty-six mothers of CHIKV-infected infants presented signs of chikungunya during the perinatal period, and onset of illness ranged from 4 days prepartum to the day after delivery (mean, −0.7 days in relation to delivery). Eighteen mothers (50%) developed clinical signs on the day of delivery. Two mothers (5%) had an asymptomatic form of the disease.

Neonatal Clinical Features. Clinical data are summarized in Table 1. Twenty-six (68%) neonates were delivered vaginally and cesarean section was performed in 12 cases (32%). Fetal heart rate abnormality was observed in 17 cases (45%). There

TABLE 1. Clinical and Laboratory Data for the 38 Neonates Studied

Observation	N (%)
Clinical	
EDIN score >3	38 (100)
Fever	30 (79)
Rash	31 (82)
Edema	22 (58)
Diarrhea	12 (32)
Seizures	6 (16)
Hemorrhagic syndrome	6 (16)
Hemodynamic disorders	10 (26)
Death	1 (3)
Laboratory	
Thrombocytopenia (<150 × 10^9/L)	29 (76)
Thrombocytopenia (<50 × 10^9/L)	12 (32)
Lymphopenia (<1 × 10^9/L)	18 (47)
Hypocalcemia (<1.9 mmol/L), n = 27	5 (19)
Prothrombin level <50%, n = 26	17 (65)
ASAT >50 IU/L, n = 30	23 (77)

EDIN indicates Echelle Douleur Inconfort Nouveau-Né, neonatal pain and discomfort scale.

were 22 boys and 16 girls. Mean gestational age was 38 weeks (range, 35–41) and mean birth weight was 3000 g (range, 1900–4010). In all infants, the first symptoms appeared between the third day of life (D3) and D7 (mean, D4). The mean interval between onset of maternal clinical signs and onset of neonatal clinical signs was 5 days (range, 3–9). Mean duration of fever was 2 days (n = 30, range, 1–8) and pain lasted for an average of 8 days (range, 2–22). Thirty-one infants developed a rash with a fairly characteristic course: initial erythroderma followed by desquamation of the extremities and, subsequently, a brownish dyschromia of the limbs and sometimes the face. Severe peripheral edema was observed in 22 cases. Most infants (n = 33) presented feeding problems requiring temporary tube feeding and 12 had diarrhea. Hemorrhagic manifestations observed were 3 gastrointestinal hemorrhages (with 1 case of necrotizing enterocolitis), 2 important intracerebral hemorrhages, and 1 case of hemorrhagic conjunctivitis. Neurologic features consisted of hypotonia (n = 17), coma, brief seizures, or status epilepticus (n = 6) during the first days of the disease. Ten neonates presented initial hemodynamic disorders.

Laboratory Tests and Complementary Investigations in Neonates. Laboratory data are summarized in Table 1. The laboratory abnormalities most frequently observed were thrombocytopenia, lymphopenia, decreased prothrombin concentration, and elevation of aspartate aminotransferase. CSF analysis was performed in 24 infants and biochemical and cytologic analysis were normal in 12 nonhemorrhagic cases. RT-PCR detection of CHIKV in CSF was positive in 22 of the 24 cases tested, including in nonhemorrhagic CSF. Head ultrasound performed in 26 neonates was pathologic in 13 cases. Precise data were available for only 7 neonates. In 5 neonates, head ultrasound demonstrated lenticulothalamostriatal vasculitis either isolated or associated with frontal or parietal periventricular hyperechogenicity (n = 4), or cerebral edema with reduction of the vascular resistance index (n = 1). MRI was performed in 25 neonates during the acute phase of the disease with abnormal findings in 14 infants. Scattered white matter lesions were found in 11 cases, including the corpus callosum in 5 cases. These lesions presented a high-intensity signal on T2-weighted sequences with reduction of the apparent diffusion coefficient (ADC) on diffusion sequences. MRI was repeated after 1 month in 8 of these 11 cases, demonstrating signal inversion on the diffusion sequence with increased ADC. Areas of intraparenchymal hemorrhage within these scattered white matter lesions were observed in 6 cases and bilateral petechial lesions were found in 4 cases. No gray matter lesions were observed. All neonates presenting convulsions had abnormal imaging.

In the group of infants undergoing systematic cardiovascular investigations (n = 16), 6 had abnormalities (Table 2). Coronary artery dilatation corresponded to unilateral or bilateral hyperechoic coronary arteries with thickened walls without aneurysmal features.

Treatment. Treatment of CHIKV-infected neonates was symptomatic. All infected neonates were admitted to a neonatal care unit or neonatal intensive care unit. The mean hospital stay was 16 days (range, 3–47). Level I analgesics (paracetamol) were prescribed in 12 cases, whereas the other 26 infants required level 2 (nalbuphine) or level 3 (morphine) analgesics. Mechanical ventilation was necessary in 9 infants (24%) with serious neurologic manifestations (status epilepticus) or multiorgan failure. Platelet (n = 9) and/or fresh frozen plasma (n = 7) transfusions were performed in neonates with hemorrhagic complications. Neonates with hemodynamic disorders required volume expansion (n = 5) and/or vasopressor amines (n = 4). Two neonates received red blood cell transfusion. One neonate died on D6 because of necrotizing enterocolitis with gastrointestinal hemorrhage and *Klebsiella pneumoniae* septicemia.

DISCUSSION

Perinatal Mother-to-Child Transmission of the CHIKV. Our series demonstrates cases of mother-to-child transmission of CHIKV infection that has never been described during previous epidemics. Mother-to-child transmission of CHIKV is highly probable for the following reasons: (1) all infected neonates were born to mothers with documented chikungunya during the perinatal period; (2) the interval between the onset of maternal and neonatal symptoms was compatible with the CHIKV incubation period; (3) no cases of such early neonatal infection were observed during the La Reunion Island epidemic without concomitant maternal infection during the days preceding delivery. The earliest cases of chikungunya observed in neonates not born to an infected mother

TABLE 2. Clinical and Complementary Cardiologic Data for 6 Cases

Case	Clinical Signs	ECG	Echocardiography	AST	Laboratory		
					CK	CKMB	TIc
1	Severe pain	RD	LVH, LVD, right/left coronary artery dilatation	250	1385	148	0.13
2	Bradycardia/desaturation, severe pain	RD	Pericarditis, LVH, right coronary artery dilatation	224	460	49	0.1
3	Heart failure, collapse	RD	Pericarditis, LVH, LVD, PHT, right/left coronary artery dilatation	172	236	62	0.15
4	Severe pain, tachycardia	RD, SVT	Right coronary artery dilatation	123	306	66	0.1
5	Severe pain, malaise	RD	LVH, right/left coronary artery dilatation	136	1417	74	0.11
6	Heart failure, collapse	RD	LVH with septal dyskinesia, right/left coronary artery dilatation	161	1284	125	1.64

RD indicates repolarization disorders; SVT, supraventricular tachycardia; LVH, left ventricular hypertrophy; LVD, left ventricular dysfunction; PHT, pulmonary artery hypertension; AST, aspartate aminotransferase (IU/L); CK, creatine kinase (IU/L); CKMB, creatine kinase, myocardial fraction (IU/L); TIc, troponin Ic fraction (ng/mL); ECG, electrocardiography.

occurred after D9 of life and probably corresponded to infections transmitted by mosquito bites soon after discharge from the maternity unit. The hypothesis of neonatal infection acquired after birth by mosquito bite during the first few hours of life needs to be considered, but, in our opinion, is extremely unlikely in European-standard air-conditioned mosquito-free maternity units.

Mother-to-child transmission of other alphaviruses has been reproduced experimentally in animals for Venezuelan equine encephalitis virus and the Semliki Forest virus[24,25] and has been described in humans for Western equine encephalitis and Venezuelan equine encephalitis viruses and is suspected for the Ross River virus.[26,27] Neonatal dengue virus infections (Flaviviridae family) with hemorrhagic complications and death have been described after perinatal transmission, with a chronology resembling that of our cases.[28]

The exact mechanisms of mother-to-child transmission of CHIKV have yet to be elucidated. Currently available data support the hypothesis of mainly perinatal transmission of CHIKV, which seems to be high, close to 50% (personal unpublished data). In the case of maternal infection during pregnancy, but occurring well before delivery, the risk of vertical transmission seems to be extremely low as only 3 cases of fetal deaths at the beginning of pregnancy have been reported during the La Reunion epidemic, and asymptomatic newborns do not seem to be infected.[29,30] Contamination during passage through the genital tract is possible, but no protective effect of cesarean section is noted in our series. Transplacental transmission shortly before delivery is the more likely mode of transmission via mother-to-child microtransfusions when the mother presents positive viremia.

Uncomplicated Neonatal Forms. Twenty-three neonates (61%) presented clinical and laboratory features of chikungunya similar to the classic form observed in adults and the disease resolved spontaneously in several days to 2 weeks. However, the benign nature of classic neonatal forms is only relative, as all CHIKV-infected neonates had to be admitted to a neonatal care unit, because of the need for fairly intensive symptomatic treatment. Furthermore, intrathecal presence of the CHIKV genome and disturbances of the cardiovascular and neurologic work-up were observed in some infants with no obvious severe complications.

Complicated Neonatal Forms. Fifteen neonates (39%) presented complicated or serious forms of chikungunya with hemorrhagic, cardiac, and neurologic manifestations.

The most serious hemorrhagic syndromes were observed in neonates with severe thrombocytopenia, disseminated intravascular coagulation, and impaired liver function. CHIKV is not usually considered to be a classic agent of "hemorrhagic fever," but such an effect has been suggested during epidemics in Southeast Asia and India.[11]

Varying degrees of severity of neurologic complications were described during the Indian epidemic of 1964: disorders of consciousness, seizures, meningeal syndromes, meningoencephalitis, transient ophthalmoplegia, and polyneuropathy.[13–15] The mechanisms of neurologic lesions have not been fully elucidated. White matter signal inversion on diffusion sequences and ADC mapping on MRI reflects the transformation of early cytotoxic edema into vasogenic edema during an interval of 1 month. No direct culture of CHIKV in CSF and no anatomopathologic examination were performed, and so the diagnosis of CHIKV viral encephalitis was not formally confirmed. Long-term follow-up of these infants is necessary to assess their neuromotor and sensory development.

Acute cardiac lesions have also been described in the course of CHIKV infection.[18–21] However, these reports were published before the age of modern imaging, and the respective roles of dengue virus and CHIKV were not always clearly distinguished. The rare pediatric series of CHIKV infection have not reported any cardiovascular complications, apart from 1 case of collapse followed by death in a 3-year-old child.[15] Coronary dilatation during other viral infections such as cytomegalovirus has recently been reported[31] but the precise mechanisms of coronary dilatation during CHIKV infection, especially the possibility of vasculitis, have not been elucidated.

Chikungunya is an arbovirus infection, which, before the La Reunion Island epidemic, was considered a benign disease. Several reasons can be proposed to explain the development of complicated forms of the disease, bearing in mind that a number of serious forms have been previously described but subsequently forgotten. The epidemic occurred on a limited territory equipped with an advanced health care and epidemiologic surveillance system allowed exhaustive identification of serious forms. This was a large-scale epidemic affecting a nonimmune population. Finally, the hypothesis of a genomic evolution of CHIKV resulting in increased virulence has also been proposed.[32]

CONCLUSIONS

The chikungunya epidemic that occurred on the La Reunion Island in 2005–2006 revealed for the first time the possibility of perinatal mother-to-child transmission of CHIKV with a high rate of neonatal morbidity. Knowledge about the clinical course along with rapid confirmation with virologic tests lead to appropriate management that can limit complications.

The absence of specific treatment justifies individual protective measures in pregnant women, particularly close to term: approved insect repellents, mosquito nets. The experience acquired in La Reunion Island and ongoing studies may be useful in other latitudes, especially as the *A. albopictus* mosquito, vector of chikungunya, is present in many regions of Europe and North America. The example of recent West Nile virus epidemics in North America demonstrates that arbovirus infections can affect new territories in nontropical zones.[33]

ACKNOWLEDGMENTS

We are grateful to Marie-Christine Jaffar-Bandjee (Service de Biologie, CHD Félix Guyon) and Alain Michault (Service de Virologie, Groupe Hospitalier Sud Réunion) for virologic work-up. We thank Gerald Rigou (Service de Radiologie, CHD Félix Guyon) and Marc Bintner (Service de Radiologie, Groupe Hospitalier Sud Réunion) for their help in interpreting the magnetic resonance images. We appreci-

ate the help of Xavier Fritel (Service de Gynécologie Obstétrique, CHD Félix Guyon) and Georges Barau (Service de Gynécologie Obstétrique, Groupe Hospitalier Sud Réunion) for obstetrical critique and discussion.

REFERENCES

1. Pialoux G, Gauzere BA, Strobel M. Infection à virus Chikungunya: revue générale par temps d'épidémie. *Med Mal Infect.* 2006;36:253–263.
2. Strauss JH, Strauss EG. The alphavirus: gene expression, replication and evolution. *Microbiol Rev.* 1994;58:491–562.
3. Robinson MC. An epidemic of virus disease in Southern Province, Tanganyka Territory, in 1952–1953. *Trans R Soc Trop Med Hyg.* 1955;49:28–32.
4. Ross RW. The Newala epidemic. III. The virus isolation, pathogenic properties and relationship to the epidemic. *J Hyg.* 1956;54:177–191.
5. Thaikruea L, Charearnsook O, Reanphumkarnkit S, et al. Chikungunya in Thailand: a re-emerging disease? *Southeast Asian J Trop Med Public Health.* 1997;28:359–364.
6. Diallo M, Thonnon J, Traore-Lamizana M, et al. Vectors of Chikungunya virus in Senegal: current data and transmission cycles. *Am J Trop Med Hyg.* 1999;60:281–286.
7. Mackenzie JS, Chua KB, Daniels PW, et al. Emerging viral diseases of Southeast Asia and the Western Pacific. *Emerg Infect Dis.* 2001;7(3 suppl):497–504.
8. Lam SK, Chua KB, Hooi PS, et al. Chikungunya infection: an emerging disease in Malaysia. *Southeast Asian J Trop Med Public Health.* 2001; 32:447–451.
9. Kennedy AC, Flemming J, Solomon L. Chikungunya viral arthropathy: a clinical description. *J Rhumatol.* 1980;7:231–236.
10. Jeandel P, Josse R, Durand JP. Arthrites virales exotiques: place des alphaviroses. *Med Trop.* 2004;64:81–88.
11. Nimmannitya S, Halstead SB, Cohen SN, et al. Dengue and Chikungunya virus infection in man in Thailand, 1962–1963. I. Observations on hospitalized patients with hemorrhagic fever. *Am J Trop Med Hyg.* 1969;18:954–971.
12. Chaudhuri RN, Chatterjea JB, Saha TK, et al. Clinical and haematological observations on a recent outbreak of dengue-like fever in Calcutta with or without haemorrhagic manifestations. *J Indian Med Assoc.* 1964;43:579–584.
13. Chatterjee SN, Chakravarti SK, Mitra AC, et al. Virological investigations of cases with neurologic complications during the outbreak of haemorrhagic fever in Calcutta. *J Indian Med Assoc.* 1965;45:314–316.
14. Thiruvengadam KV, Kalyanasundaram V, Rajgopal J. Clinical and pathological studies on Chikungunya fever in Madras city. *Indian J Med Res.* 1965;53:729–744.
15. Jadhav M, Namboodripad M, Carman RH, et al. Chikungunya disease in infants and children in Vellore: a report of clinical and haematological features of virologically proved cases. *Indian J Med Res.* 1965;53:764–776.
16. Sarkar JK, Chatterjee SN, Chakravarti SK, et al. Chikungunya virus infection with haemorrhagic manifestations. *Indian J Med Res.* 1965; 53:921–925.
17. Carey DE, Myers RM, DeRanitz CM, et al. The 1964 Chikungunya epidemic at Vellore, South India, including observations on concurrent dengue. *Trans R Soc Trop Med Hyg.* 1969;63:434–445.
18. Munasinghe DR, Amarasekera PJ, Fernando CFO. An epidemic of dengue-like fever in Ceylon (Chikungunya). A clinical and haematological study. *Ceylon Med J.* 1966;11:129–142.
19. Obeyesekere I, Hermon Y. Myocarditis and cardiomyopathy after arbovirus infection (dengue and chikungunya fever). *Br Heart J.* 1972;34: 821–827.
20. Obeyesekere I, Hermon Y. Arbovirus heart disease: myocarditis and cardiomyopathy following dengue and chikungunya fever. A follow up study. *Am Heart J.* 1973;85:186–194.
21. Maiti CR, Mukherjee AK, Bose B, Saha GL. Myopericarditis following Chikungunya infection. *J Indian Med Assoc.* 1978;70:256–258.
22. Robillard PY, Boumahni B, Gerardin P, et al. Transmission matemo-fœtale du virus chikungunya. *Presse Med.* 2006;35:785–788.
23. Pastorino B, Bessaud M, Grandadam M, et al. Development of a TaqMan® RT-PCR assay without RNA extraction step for the detection and quantification of African Chikungunya viruses. *J Virol Methods.* 2005;124:65–67.
24. Garcia-Tamayo J, Esparza J, Martinez AJ. Placental and fetal alterations due to Venezuelan equine encephalitis virus in rats. *Infect Immun.* 1981;32:813–821.
25. Atkins GJ, Carter J, Sheanhan BJ. Effect of alphavirus infection on mouse embryos. *Infect Immun.* 1982;38:1285–1290.
26. Aaskov JG, Nair K, Lawrence GW, et al. Evidence for transplacental transmission of Ross River virus in humans. *Med J Aust.* 1981;2:20–21.
27. Aleck KA, Rosen L, Pettitt DJ, et al. Absence of intrauterine infection following Ross River virus infection during pregnancy. *Am J Trop Med Hyg.* 1963;32:618–620.
28. Sirinavin S, Nuntnarumit P, Supapannachart S, et al. Vertical dengue infection: case reports and review. *Pediatr Infect Dis J.* 2004;23:1042–1047.
29. Lenglet Y, Barau G, Robillard PY, et al. Infection à Chikungunya chez la femme enceinte et risque de transmission materno-fœtale. *J Gynecol Obstet Biol Reprod.* 2006;35:578–583.
30. Touret Y, Randrianaivo H, Michault A, et al. Transmission matemo-fœtale précoce du virus chikungunya. *Presse Med.* 2006;35:1656–1658.
31. Catalano-Pons C, Quartier P, Leruez-Ville M, et al. Primary cytomegalovirus infection, atypical Kawasaki disease and coronary aneurysm in 2 infants. *Clin Inf Dis.* 2005;41:e53–e56.
32. Schuffenecker I, Iteman I, Michault A, et al. Genome microevolution of chikungunya viruses causing the Indian Ocean outbreak. *PLoS Med.* 2006;3:e263.
33. Jamieson DJ, Jernigan DB, Ellis JE, Treadwell TR. Emerging infections and pregnancy: West Nile virus, monkeypox, severe acute respiratory syndrome, and bioterrorism. *Clin Perinatol.* 2005;32:765–776.