Viewpoint

Non vector-borne transmission modes of dengue

Viroj Wiwanitkit

Wiwanitkit House, Bangkhae, Bangkok Thailand 10160

Abstract

Dengue is the most important tropical mosquito-borne infectious disease caused by an arbovirus, the dengue virus. It should be noted that there are still other unusual modes of transmission of dengue infection. This paper summarizes those non vector-borne transmissions of dengue including vertical transmission, transfusion related transmission, transplantation related transmission, and needle-stick-related transmission.

Key words: transmission, dengue, unusual

J Infect Dev Ctries 2010; 4(1):051-054.

(Received 7 June 2009 – Accepted 29 November 2009)

Introduction

Dengue is an important tropical mosquito-borne infectious disease [1,2]. It is highly prevalent in tropical Asia, especially Southeast Asia [3]. The *Aedes* species mosquito is the most significant vector for dengue infection [1]. After being bitten by a vector mosquito, human beings will obtain the dengue virus, which can result in infection. The dengue virus is a single-stranded RNA virus in the genus *Flavivirus* and family Flaviviridae. This virus is approximately 40-60 nm [1,2]. There are four distinct serotypes of dengue virus that can cause disease. A high fever, accompanied by hemoconcentration and thrombocytopenia, is the hallmark of severe dengue disease [1].

It should be noted that there remain other non vector-borne modes of dengue transmission. These uncommon modes of transmission are identified as vertical transmission from mother to fetus, transfusion-related transmission, transplantation-related transmission, and needle-stick-related transmission. This paper summarizes those non vector-borne transmissions of dengue.

Vertical transmission

Similar to many other infectious diseases, pregnant women can get dengue infection [5,6]; hence, pregnant women should avoid getting dengue infection to prevent the possibility of vertical transmission. The query is how dengue virus can be transmitted to the foetus and further cause congenital infection [7]. This problem should be discussed into two parts. In case of early pregnancy, there is no evidence for vertical transmission. In case of late pregnancy, there is some confirmative evidence [8,12]. It is confirmed that near-term pregnant women who are infected with dengue virus can transmit the disease to the foetus through the placenta and this can result in congenital infection. The dengue virus, an RNA virus, has a small molecular size (about 40 – 60 nm) [13] that can permit vertical transmission of disease, which is concordant with the basic rule of vertical transmission in nanomedicine [14]; however, there is still the question of why there is no problem in cases of early pregnancy despite the fact that placenta might exist. This might be due to the incomplete development of the immune system of the foetus. It should be clarified that immunopathogenesis is proposed to be the main possible pathogenesis leading to congenital dengue infection [8,9]. In the neonate with congenital dengue infection, the passed dengue virus from the mother might stimulate the antibody response and further induce thrombocytpenia via possible autoimmune mechanisms [15,18].

Transfusion-related transmission

Since dengue virus can be classified as a blood pathogen, there is a stage of viremia in dengue. If blood is donated in this condition, infection of the recipients of the contaminated blood can be expected [19,25]. There are many reports of transfusion-related

transmission of dengue [19,25]. According to a recent report from Hong Kong, the prevalence of this mode of the transmission of dengue stands at one in 126 [24]. This statistical detail needs attention, particularly because the problem that it identifies can be controlled effectively by implementing a basic-practice blood-donation procedure that disallows the donations of dengue fever-infected donors. Dengue-infected cases in the viremic stage usually exhibit a high fever and are therefore easily detected by standard blood donor screening.

However, asymptomatic and pre-symptomatic cases are important in transfusion-related transmission [26,27] and should be investigated. Asymptomatic and pre-symptomatic cases can easily evade the basic screening of the blood donation process. In an Indonesian study using a cluster sampling of index dengue cases, eight of the 785 studied cases revealed asymptomatic dengue infection [26], and nine of symptomatic infection. Recently, de Lourdes Garza Rodríguez *et al*. also noted a similarly high rate of asymptomatic dengue virus-infected blood donors (16/800) [27]. Another report from Colombia confirmed viral isolation at 6.7% of the studied population in endemic areas. Interestingly, most of the detected cases were asymptomatic [28]. These reports confirm the importance of asymptomatic dengue cases in transfusion-related transmission. There is presently no routine practice in any blood centres, including those in dengue endemic areas, for screening of the dengue virus in donated blood [22]; nevertheless, Mohammed *et al*. reported a high rate of dengue virus contamination in donated blood and suggested the need for routine screening [22]. It should also be noted that there is no evidence of whether routine blood radiation can get rid of the contaminated dengue virus. Xi *et al*. recently reported a new viral inactivation and removal approach that was successful in eliminating the dengue virus within plasma-derived proteins (*e.g.* albumin and immunoglobulin). This technique uses cold ethanol precipitation, cation-exchange chromatography, pasteurization, solvent-detergent treatment, and virus filtration [29]; therefore, pathogen inactivation treatment of platelet concentration and packed red blood cells is another method of improving blood safety. Photochemical treatment is clinically useful in eliminating the contaminated dengue virus [30,31]. Psoralen S-59 and long-wavelength ultraviolet light (UVA, 320-400 nm) are used for generating photochemical reaction [32]. The photochemical treatment can also reduce the rate of acute transfusion reaction [32]. Finally, it should be noted that primary exclusion of the donor is the important factor in preventing transfusion-related transmission of the dengue virus.

Transplantation-related transmission

At present, organ transplantation is the new hope for treatment of many serious diseases. Similar to the blood transfusion process, some pathogens can be transmitted via the organ transplantation process. Transplantation-related transmission of the dengue virus has been confirmed previously [33,34]. There are two reports: one case of transplantation-related transmission with renal transplantation [33] and one with bone marrow transplantation [34]. In the organ transplantation process, there is no screening for dengue virus even though there are many required tests for screening for the donated organs for possible contamination of infectious agents.. There is ample evidence from fatal cases confirming that the dengue virus can be isolated and detected in several organs [35,37]; however, it is not completely understood whether the dengue virus is located in these organs in asymptomatic and pre-symptomatic cases. Indeed, this mode of transmission of dengue is not common since the infected organs must be derived from a dengue-infected donor who must be at the viremic stage. This is also the reason that there are only a few reports of this unusual mode of transmission of dengue. Good donor screening systems seem to be the best preventive method for transplantation-related transmission.

Needle-stick-related transmission

Needle-stick injury is one of the most common accidents in routine medical practice. It is confirmed that needle-stick injury can cause several possible infectious diseases to the victim of the accident [38]. Several infectious diseases, including human immunodeficiency virus (HIV) infection and hepatitis B, are transmittable via needlestick injury [39]. Dengue has been confirmed in needle-stick-related transmission events. At present, there are less than ten reports of this mode of transmission of dengue [40,43]. This mode of transmission of dengue is very rare and the patients are usually medical personnel, not the general population, because medical personnel are the main group of people who use needles. For transmitted cases, serious injuries are common. In general, the amount of dengue virus necessary to infect a subject naturally, via the

mosquito route, can be as few as 10 to 20 copies of the virus [44,46]; however, in the case of needle-stick-related transmission, more than this quantity of the virus might be required. There must be a high level of virus in the viremic donor and an appropriately large amount of contaminated blood must enter into the wound of the severely injured medical personnel who suffered the needle stick. Compared to the case of needle-stick-related transmission of HIV, which requires up to 500 copies of the virus, similar low levels of the dengue virus can result in infection in the usual route of transmission [47]. In conclusion, nosocomial mucocutaneous transmission of dengue among health care workers should not be forgotten. The standard precautions for needle-stick injuries are the best preventive measures for needle-stick-related transmission of dengue [4, 48].

Conclusions

Dengue is an important tropical mosquito-borne infectious disease. Similar to other flaviviruses, it should be noted that there remain other non vector-borne modes of transmission of the dengue virus. This paper summarizes the most important aspects of non vector-borne modes of dengue transmission that might be underestimated in endemic areas, including vertical transmission, transfusion-related transmission, transplantation-related transmission, and needle-stick-related transmission. Vertical transmission is confirmed and should be a differential diagnosis of febrile infants with thrombocytopenia. Transfusion and transplantation modes are not unusual and can be the problems in transfusion and transplantation medicine. Donor screening is an important factor in ensuring safety. Regarding needle-stick-related transmission, dengue can be a nosocomial infection and should be an important concern in occupational medicine. Since these abnormal transmissions are possible and usually neglected, it is necessary that general practitioners in dengue endemic areas not forget these probable modes of transmission. The impact of these probable underreported transmissions in dengue endemic/epidemic developing countries should be noted since there can be several under-diagnosed cases of dengue due to these unusual modes of transmission.

References

1. Heymann WR (2009) Dengue fever. J Am Acad Dermatol 60: 306-307.
2. Halstead SB (2007) Dengue. Lancet 370: 1644-1652.
3. Ooi EE and Gubler DJ (2009) Dengue in Southeast Asia: epidemiological characteristics and strategic challenges in disease prevention. Cad Saude Publica 25 Suppl 1: S115-124.
4. Chen LH and Wilson ME (2004) Transmission of dengue virus without a mosquito vector: nosocomial mucocutaneous transmission and other routes of transmission. Clin Infect Dis 39: e56-60.
5. Carroll ID, Toovey S, Van Gompel A (2007) Dengue fever and pregnancy - a review and comment. Travel Med Infect Dis 5: 183-188.
6. Waduge R *et al*. (2006) Dengue infections during pregnancy: a case series from Sri Lanka and review of the literature. J Clin Virol 37: 27-33.
7. Wiwanitkit V (2006) Dengue haemorrhagic fever in pregnancy: Appraisal on Thai cases. J Vector Borne Dis 43: 203-205.
8. Sirinavin S, *et al*. (2004) Vertical dengue infection: case reports and review. Pediatr Infect Dis J 23: 1042-1047.
9. Fatimil LE, Mollah AH, Ahmed S, Rahman M (2003) Vertical transmission of dengue: first case report from Bangladesh. Southeast Asian J Trop Med Public Health 34: 800-803.
10. Chotigeat U, Kalayanarooj S, Nisalak A (2003) Vertical transmission of dengue infection in Thai infants: two case reports. J Med Assoc Thai 86 Suppl 3: S628-632.
11. Boussemart T, Babe P, Sibille G, Neyret C, Berchel C (2001) Prenatal transmission of dengue: two new cases. J Perinatol 21: 255-257.
12. Chye JK, *et al*. (1997) Vertical transmission of dengue. Clin Infect Dis 25: 1374-1377.
13. Harris E, Holden KL, Edgil D, Polacek C, Clyde K (2006) Molecular biology of flaviviruses. Novartis Found Symp 277: 23-39.
14. Wiwanitkit V (2006) New emerging blood-borne hepatitis viral pathogens and the feasibility of passing thorough the placenta: An appraisal. Clin Expl Ob Gyn 33: 213-214.
15. Kurane I (2007) Dengue hemorrhagic fever with special emphasis on immunopathogenesis. Comp Immunol Microbiol Infect Dis 30: 329-340.
16. Wiwanitkit V (2005) Weak binding affinity of immunoglobin G, an explanation for the immune mimicking theory in pathophysiologic findings in the recovery phase of dengue. Nanomedicine 1: 239-240.
17. Lei HY, *et al*. (2001) Immunopathogenesis of dengue virus infection. J Biomed Sci 8: 377-388.
18. Lin CF, Wan SW, Cheng HJ, Lei HY, Lin YS (2006) Autoimmune pathogenesis in dengue virus infection. Viral Immunol 19: 127-132.
19. Seed CR, Kiely P, Hyland CA, Keller AJ (2009) The risk of dengue transmission by blood during a 2004 outbreak in Cairns, Australia. Transfusion [Epub ahead of print].
20. Teo D, Ng LC, Lam S (2009) Is dengue a threat to the blood supply? Transfus Med 19: 66-77.
21. Wilder-Smith A, Chen LH, Massad E, Wilson ME (2009) Threat of dengue to blood safety in dengue-endemic countries. Emerg Infect Dis 15: 8-11.
22. Mohammed H, *et al*. (2008) Dengue virus in blood donations, Puerto Rico, 2005. Transfusion 48: 1348-1354.
23. Linnen JM, *et al*. (2008) Dengue viremia in blood donors from Honduras, Brazil, and Australia. Transfusion 48: 1355-1362.
24. Chuang VW, *et al*. (2008) Review of dengue fever cases in

Hong Kong during 1998 to 2005. Hong Kong Med J 14: 170-177.
25. Tambyah PA, Koay ES, Poon ML, Lin RV, Ong BK (2008) Transfusion-Transmitted Dengue Infection Study Group. Dengue hemorrhagic fever transmitted by blood transfusion. N Engl J Med 359: 1526-1527.
26. Beckett CG, *et al*. (2005) Early detection of dengue infections using cluster sampling around index cases. Am J Trop Med Hyg 72: 777-782.
27. de Lourdes Garza Rodríguez M, *et al*. (2009) Serologic Surveillance for West Nile Virus and Other Flaviviruses in Febrile Patients, Encephalitic Patients, and Asymptomatic Blood Donors in Northern Mexico. Vector Borne Zoonotic Dis [Epub ahead of print].
28. Méndez F, *et al*. (2006) Human and mosquito infections by dengue viruses during and after epidemics in a dengue-endemic region of Colombia. Am J Trop Med Hyg 74: 678-683.
29. Xie YW, *et al*. (2008) Clearance of dengue virus in the plasma-derived therapeutic proteins. Transfusion 48: 1342-1347
30. Teo D, Ng LC, Lam S (2009) Is dengue a threat to the blood supply? Transfus Med 19: 66-77.
31. Lam S, *et al*. (2007) Efficacy of INTERCEPT treatment for the inactivation of dengue virus in single-donor platelet concentrate. Transfusion 47(S3): 131A – 2[a]
32. Rasonglès P, *et al*. (2009) Transfusion of platelet components prepared with photochemical pathogen inactivation treatment during a Chikungunya virus epidemic in Ile de La Réunion. Transfusion 49: 1083-1091.
33. Tan FL, Loh DL, Prabhakaran K, Tambyah PA, Yap HK (2005) Dengue haemorrhagic fever after living donor renal transplantation. Nephrol Dial Transplant 20: 447-448.
34. Rigau-Pérez JG, Laufer MK (2006) Dengue-related deaths in Puerto Rico, 1992-1996: diagnosis and clinical alarm signals. Clin Infect Dis 42: 1241-1246.
35. Limonta D, Capó V, Torres G, Pérez AB, Guzmán MG (2007) Apoptosis in tissues from fatal dengue shock syndrome. J Clin Virol 40: 50-54.
36. Limonta D, *et al*. (2009) Fatal severe dengue and cell death in sickle cell disease during the 2001-2002 Havana dengue epidemic. Int J Infect Dis 13: e77-78.
37. Nogueira RM, *et al*. (2005) Dengue virus type 3, Brazil, 2002. Emerg Infect Dis 11: 1376-81.
38. Trim JC and Elliott TS (2003) A review of sharps injuries and preventative strategies. J Hosp Infect 53: 237-242.
39. Thompson SC, Boughton CR, Dore GJ (2003) Blood-borne viruses and their survival in the environment: is public concern about community needlestick exposures justified? Aust N Z J Public Health 27: 602-607.
40. Wagner D, *et al*. (2004) Nosocomial acquisition of dengue. Emerg Infect Dis 10: 1872-1873.
41. Langgartner J, Audebert F, Schölmerich J, Glück T (2002) Dengue virus infection transmitted by needle stick injury. J Infect 44: 269-270.
42. de Wazières B, Gil H, Vuitton DA, Dupond JL (1998) Nosocomial transmission of dengue from a needlestick injury. Lancet 351: 498.
43. Nemes Z, *et al*. (2004) Nosocomial transmission of dengue. Emerg Infect Dis 10: 1880-1881.
44. Gurukumar KR, *et al*. (2009) Development of real time PCR for detection and quantitation of dengue viruses. Virol J 6: 10.
45. Wang WK, *et al*. (2002) Detection of dengue virus replication in peripheral blood mononuclear cells from dengue virus type 2-infected patients by a reverse transcription-real-time PCR assay. J Clin Microbiol 40: 4472-4478.
46. Richardson J, Molina-Cruz A, Salazar MI, Black W 4[th] (2006) Quantitative analysis of dengue-2 virus RNA during the extrinsic incubation period in individual Aedes aegypti. Am J Trop Med Hyg 74: 132-141.
47. Kraiselburd E, Gubler DJ, Kessler MJ (1985) Quantity of dengue virus required to infect rhesus monkeys. Trans R Soc Trop Med Hyg 79: 248-251
48. Chen LH and Wilson ME (2005) Nosocomial dengue by mucocutaneous transmission. Emerg Infect Dis 11: 775.

Corresponding Author
Professor Viroj Wiwanitkit, MD
Wiwanitkit House, Bangkhae, Bangkok Thailand 10160
Phone: 6624132436, Fax: 6624132436
Email: wviroj@yahoo.com

Conflict of interest: No conflict of interest is declared.