The tainted milk of human kindness

Dominique Goedhals, Inéz Rossouw, Ute Hallbauer, Mitta Mamabolo, Tulio de Oliveira

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Department of Medical Microbiology and Virology, National Health Laboratory Service (D Goedhals MMed [Virol], I Rossouw MMed [Virol], M Mamabolo BSc), **and Department of Pediatrics and Child Health** (U Hallbauer FC Paed SA), **University of the Free State, Bloemfontein, South Africa and; Africa Centre for Health and Population Studies, University of KwaZulu-Natal, Mtubatuba, South Africa and; Research Department of Infection, Division of Immunity, University College London, London, UK** (T de Oliveira PhD)

Correspondence to:
Dr Dominique Goedhals, Department of Medical Microbiology and Virology, University of the Free State, Box 339 (G23), Bloemfontein, South Africa, 9300
gnvrdg@ufs.ac.za

or

Dr Tulio de Oliveira, PO Box 198, Mtubatuba, 3935, South Africa
tdeoliveira@africacentre.ac.za

See Online for appendix

In September, 2009, a 74-day-old infant presented to a local hospital in Bloemfontein, South Africa, in bronchopneumonia related respiratory distress. She appeared pale, cyanosed, and had palpable axillary lymph nodes, hepatomegaly, and oropharyngeal candidosis. She had received all scheduled vaccinations and had been exclusively breastfed. Cytomegalovirus was isolated from a respiratory sample by shell vial culture, and a paired blood sample showed a cytomegalovirus viral load of 12 600 copies per mL. She was positive for HIV by ELISA and DNA PCR. However, the baby's mother said that she tested HIV negative during pregnancy, which was confirmed by fourth generation ELISA test. The baby's CD4 cell count was 2189×10^6 cells per L (40% lymphocytes) and antiretroviral therapy was started. The mother reported that her sister had breastfed the baby intermittently from 6 weeks of age. The sister and her 5-month-old child were subsequently found to be HIV positive by ELISA and DNA PCR. Laboratory records confirmed the sister's positive HIV status in February, 2008, excluding recent seroconversion. At final follow-up in April, 2010, our patient was well with an undetectable HIV viral load (see appendix).

Plasma samples from the sister and both infants were used for partial sequencing of the HIV *pol* gene with the TRUGENE HIV-1 genotyping kit (Siemens Healthcare Diagnostics, Tarrytown, NY, USA). We analysed the data with the same approach used to identify the source of the nosocomial HIV-1 CRFO2_AG outbreak in the Al-Fateh Hospital, Libya.[1] We collated 100 HIV-1 reference strains from the Free State Province, South Africa, closely related to the three case sequences, and then estimated and assessed phylogenies using algorithmic, Bayesian, and maximum-likelihood methods. The case sequences form a well-supported monophyletic cluster within the HIV-1 subtype C clade. The linkage is supported with 100% bootstrap in the algorithm and maximum-likelihood methods and with 100% posterior probability in the Bayesian phylogenies (figure). The branch length leading is long and typical of a transmission cluster. In addition, a phylogenetic tree of 1800 subtype C sequences sampled globally confirmed the smaller phylogeny results (appendix). This supported the scenario of surrogate transmission between the sister and her niece, although the direction of transmission cannot be determined. The short branch length connecting the three sequences and low diversity suggest a recent transmission event.

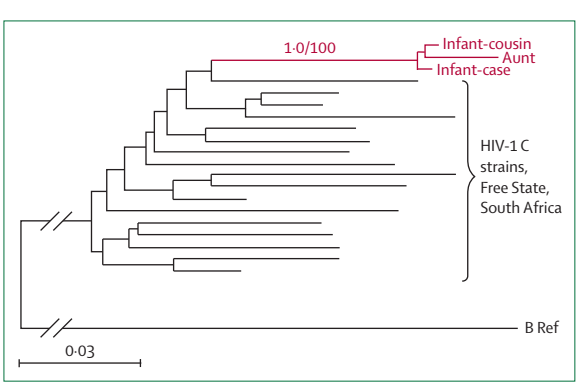

Figure: **HIV-1 Consensus Majority Rule Bayesian Tree showing posterior probabilities for the internal branch of the tree that connect the three case sequences.** Scale bar units are nucleotide substitutions per site. Sequences from the transmission case are shown in red; the tree is rooted with the HIV-1 subtype B reference sequence; the sub tree phylogeny contains 17 of remaining 107 sequences that are the most similar HIV-1 subtype C sequences in the Free State.

Acute retroviral syndrome is noted in 40–90% of adults with acute HIV infections, but is less frequently described in children. Lymphadenopathy, hepatomegaly, pneumonia and oropharyngeal candidosis in our patient are consistent with acute retroviral syndrome.[2] The time of presentation is also consistent with the likely route of transmission, with an interval of about 4–5 weeks after she was first reportedly breastfed by her aunt. HIV transmission via breastfeeding has been well described, with the probability of transmission per litre of ingested breastmilk reported to be similar to that of a heterosexual contact.[3] The scarce information available suggests that 1% of infants in South Africa are breastfed by a surrogate.[4] However, results from a study in the Free State Province, South Africa, showed that shared breastfeeding by a non-biological caregiver was the most important factor associated with HIV infection in discordant mother–child pairs.[5] Our case highlights the importance of continued education about the risk of HIV transmission via surrogate breastfeeding and the implementation of safe and appropriate infant feeding practices, including HIV testing of all breastfeeding surrogates, especially in view of the decision to halt the provision of formula feeds at public health facilities in South Africa.

Contributors
UH looked after the patient; DG, IR, and UH collected the data; DG and MK did the laboratory testing; TdO analysed the data; all authors wrote the report.

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