

An HIV-1 Transmission Case Possibly Associated with Manicure Care

Elaine Monteiro Matsuda,¹ Luana Portes Ozório Coelho,² Victor Figueiredo Pimentel,³
Humberto Barjud Onias,¹ and Luís Fernando de Macedo Brigido²

Abstract

A recently diagnosed 22-year-old female with no history of transmission risk factors prompted a thorough investigation of possible alternative risk factors. As the patient had evidence of advanced disease and laboratory data compatible with long-standing infection, past events were reviewed. About 10 years ago the patient shared manicure utensils with an older cousin, later known to be HIV infected; this prompted the phylogenetic analysis of the HIV sequences of both patients. Phylogenetic analyses of partial HIV-1 polymerase and envelope sequences from both patients revealed highly related sequences, with an estimated common ancestor date (about 11 years ago) that coincided with the putative sharing of manicure instruments, during a time in which the cousin was not virally suppressed. Taken together, the information about the infection of this patient suggests the use of shared manicure instruments as an alternative route of fomite HIV-1 transmission.

THE CONCEPT THAT PARAPHERNALIA may mediate HIV acquisition is not new,¹ but with the ubiquity of sexual activity, the major driver of new infections, alternative, non-classical modes of transmission may be overlooked. Body fluids, especially blood, can contaminate different instruments and lead to fomite transmission. Among potential sources, negligence in using beauty instruments such as needles for tattooing and razors may increase viral transmission, especially hepatitis C.² Even when safe practices are enforced at the work environment, home use of these tools may represent a risk, as some decontaminating steps may not be enforced. We describe a case of HIV infection potentially related to the use of cuticle scissors or other manicure care instruments.

A 22-year-old Brazilian woman, diagnosed with HIV infection after a first blood donation, was evaluated at the HIV/AIDS outpatient clinic, Santo Andre Infectious Diseases Ambulatory, Brazil. The patient (case) denied vaginal, anal, or oral sexual intercourse, blood transfusion, surgery, piercing, or tattooing. She had a boyfriend (seronegative by rapid check HIV test) for 2 years, but still had not engaged in sexual intercourse (a gynecological examination in August 2014 is compatible with the patient's statements). Her mother (seronegative by rapid check HIV test) confirmed that she was her biological mother and that the patient had never used blood products in childhood and had never suffered sexual violence. The patient reported no symptoms, but physical

examination revealed oral candidiasis. She had an otherwise normal laboratory workup except for a low platelet count (115,000/ml), a low CD4 count (11 cells/mm³), and a viral load of 64,966 copies/ml (log 4.81).

Fluconazol and lamivudine/tenofovir/lopinavir/ritonavir were introduced. As the patient had no apparent transmission risk factor, a comprehensive review of all possible HIV acquisition routes was discussed independently by three attending physicians during subsequent visits. The only plausible mode of transmission was associated with events, about 10 years ago, when she remembered that at the age of 12 she used manicure instruments, including cuticle scissors, from an HIV-infected cousin. At that time the family did not know about the cousin's HIV infection. The cousin (putative index case, PIC) is a patient at the same clinic. She is a female manicurist, age 36 years, who was diagnosed 17 years ago during her third pregnancy. After she was diagnosed with HIV she used zidovudine and lamivudine until delivery, but was subsequently lost from follow-up. PIC remained without treatment for 5 years (1997–2003), a period that included the time of the putative transmission event. PIC did not remember any specific sharing event, but the case and her mother confirmed the occasional use of PIC's manicure instruments at home. Any other plausible risk, including any kind of relationship with a third party, as a common male partner, was denied. PIC was probably contaminated by the

¹Santo André Aids Program, São Paulo, SP, Brazil.

²Retrovirus Laboratory, Virology Center, Adolfo Lutz Institute, São Paulo, SP, Brazil.

³University of São Paulo, São Paulo, SP, Brazil.

father of her third child, with whom she did not have a stable relationship. He did not partake of the family environment, making the possibility of sexual abuse unlikely, in agreement with the patient's and her mother's statements.

In 2003, PIC started zidovudine/lamivudine/nevirapine during her fourth pregnancy. Her first viral load, tested 10 days into treatment, was 7,530 copies/ml (log 3,88); it remained below the limit of detection until March 2008, when due to virological failure associated with irregular use of therapy, tenofovir/lamivudine/atazanavir/ritonavir was introduced. PIC has maintained undetectable viremia until her last evaluation in 2014.

Biological material was obtained after informed consent on separate occasions from both patients and processed and evaluated at the retrovirus laboratory, Adolfo Lutz Institute. Both patients had DNA from cell and RNA from plasma extracted and polymerase chain reaction (PCR) amplified in separate procedures, with the *env* and *pol* regions sequenced as previously described^{3,4} (Supplementary Methods; Supplementary Data are available online at www.liebertpub.com/aid). PIC was undetectable at the time and only cell-associated HIV genetic material (proviral DNA) was amplified and sequenced, with HIV sequences obtained from cell and plasma for the case. Phylogenetic analyses of the *pol* and *env* sequences from both patients revealed highly related HIV

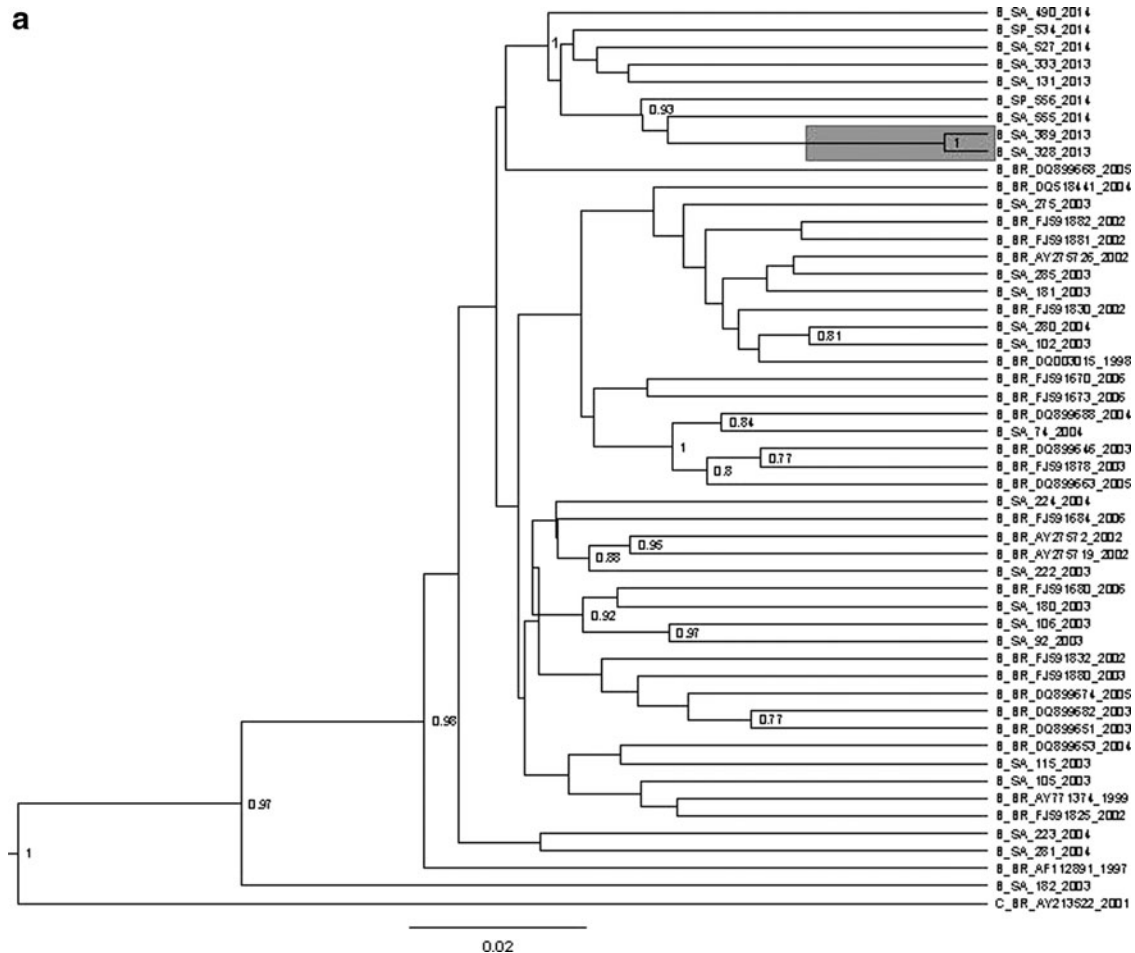


FIG. 1. Phylogenetic trees of HIV-1 genome segments *pol* PR/RT (~780 pb) and *env* c2-v3 (~500 pb). B-Markov Chain Monte Carlo (MCMC) phylogenetic trees were constructed using the GTR + I + Γ model, based on four independent MCMC runs of four chains each, run for 20 million generations, combined using LogCombiner after the consensus tree was obtained with TreeAnnotator. **(a)** Fifty-two sequences from HIV-1 subtype B were analyzed along with one subtype C, used to root the tree. Sequences included those obtained from the two study patients, from available sequences from the same clinical service (SA), from other areas in São Paulo (SP), and from other Brazilian sequences at GenBank (BR). Sequences are coded as subtype (B or C), place of isolation, laboratory or GenBank number, and date of collection. Sequences from study patients are highlighted by a gray box. The tree was rooted using one HIV subtype C sequence (AY213522). [Only key nodes with a high (>0.70) posterior probability (PP) support are displayed on the tree.] **(b)** Available subtype B partial envelope sequences from Brazil at GenBank along with HIV-1 B sequences from study patients and sequences from other patients from the same city (SA) were named and analyzed as described above. Moreover, we estimated the time of the most recent common ancestor (TMRCA) under a Bayesian skyline coalescent tree, which is shown for the main nodes. The rectangle, highlighted in gray, represents the sequences of both study patients, with a high PP (1.0), and an estimated common ancestor date about 10.81 years ago. The tree was rooted using two HIV-1 subtype C reference sequences (AB254149 and AY727523).

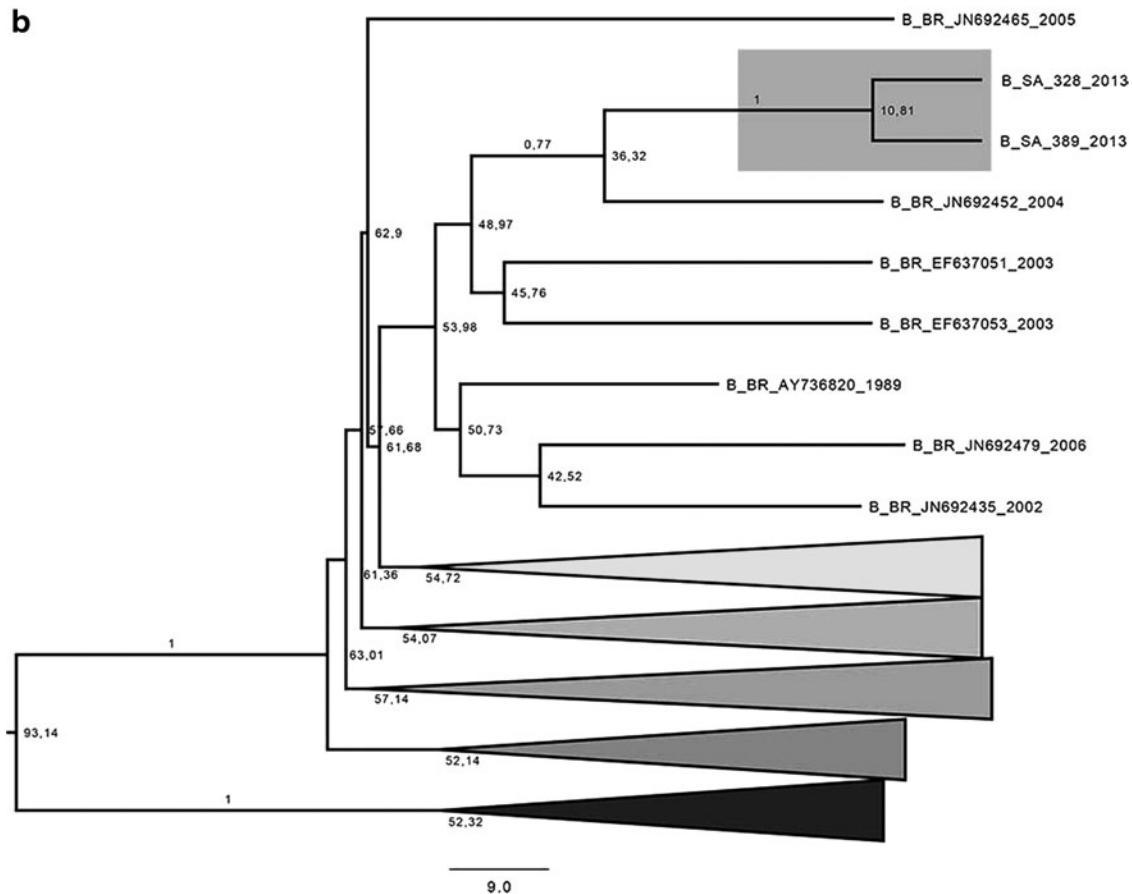


FIG. 1. (Continued).

sequences, with a pairwise nucleotide identity of 0.966% at *pol* and of 0.948% at *env* (0.914% considering gaps/insertions). Evaluation of *pol* at the Stanford database shows a similar mutation pattern, but some additional mutations at the PIC sequence predicted a low level resistance to nelfinavir and saquinavir and potential low level resistance to atazanavir and indinavir. The mutations identified in both patients at protease included L33I, R41K, I64V, H69Y, V77I, and I93L and at reverse transcriptase (RT) I50V, K122E, and E169D. No additional mutations were observed in the case at protease, with K20R, K22R, and F214 at RT. In PIC, G73S and G86R were additionally observed at protease and at RT M41I, K49R, and R211K. Both patients had a predicted CCR5 only tropism (geno2pheno false-positive rate of 21% for the case and 39% for PIC).

Figure 1 depicts phylogenetic trees, constructed using BEAST v1.7.4, under the GTR+I+ Γ model (Fig. 1a polymerase and Fig. 1b envelope). Four Markov Chain Monte Carlo (MCMC) runs were done independently; each MCMC run was 20,000,000 generations and was resampled every 2,000 generations. The runs were combined using LogCombiner after the consensus tree was obtained with TreeAnnotator. Trees were rooted with HIV-1 subtype C reference.

A representative *pol* phylogenetic tree was built using study cases and available sequences from naive and treated HIV-infected individuals followed at the same clinic, along with sequences from other areas of São Paulo and GenBank

references (Fig. 1a). To trace the lineage of patients' sequences back in time, we evaluated *env* sequences with B-MCMC,⁵ along with available subtype B envelope sequences from Brazil at GenBank covering position 6,800 to 7,500, excluding clones. Available HIV sequences obtained from other patients at the same clinic were also included, along with two subtype C references to root the tree (Fig. 1b). The estimated common ancestor date (about 11 years ago) corresponds to the period of the referred sharing of manicure instruments, a time when PIC was not virally suppressed. Sequences are available at GenBank with accession numbers KM360099 to KM360119 and KM489108 to KM489123.

With the phylogenetic data on hand, the case and PIC were further interviewed and the epidemiological data were confirmed. Although it is very difficult to determine the course of events occurring a decade ago and to guarantee that the use of the cosmetic paraphernalia was actually the mode of transmission, the HIV envelope and polymerase regions from both women are strongly related by phylogenetic parameters, and no alternative mode of transmission was identified. In a recent case of transmission among women, the CDC lists, along classical transmission routes, potential alternative sources that must be ruled out, such as tattooing, acupuncture, piercing, the use of shared sex toys between the partners and other persons, and exposure to body fluids,⁶ but does not include manicure instruments. Our case raises the potential role of an additional fomite-related route of transmission of HIV-1.

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Author Disclosure Statement

No competing financial interests exist.

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Address correspondence to:
Luís Fernando de Macedo Brígido
Retrovirus Laboratory
Virology Center
Adolfo Lutz Institute
Ave. Dr. Arnaldo 355
São Paulo 01246-902
Brazil

E-mail: lubrigido@gmail.com