Infezione da HIV in una donna ucraina di 22 anni riscontrata al parto: case report.

HIV infection in a 22-year-old treatment-naïve Ukrainian woman at delivery: a case report.

Cinzia R. Bassoli[1], Giada Canavesi[1,2], Laura Pezzati[1], Francesco Bassani[1,2], Dario Bernacchia[1], Gabriele Pagani[1], Marco Franzetti[1], Cristina Basilico[1], Maurizio Mena[1], Massimo P. Villa[1], Massimo De Paschale[3], Claudia Pavia[3], Valeria Micheli[4], Stefano Rusconi[1,5]

[1] Infectious Diseases Unit, Legnano Hospital, ASST Ovest Milanese, Legnano, Italy
[2] Università degli Studi di Milano, Milan, Italy
[3] Microbiology Unit, Legnano Hospital, ASST Ovest Milanese, Legnano, Italy
[4] L. Sacco University Hospital, ASST Fatebenefratelli Sacco, Laboratory of Clinical Microbiology, Virology, and Bioemergencies, Milan, Italy
[5] DIBIC, Università degli Studi di Milano, Italy

Riassunto

Dall'inizio dell'epidemia di HIV al 31 Dicembre 2022 in Italia sono stati riportati 742 casi di infezione pediatrica trasmessa per via verticale, nonostante siano stati istituiti programmi di screening per HIV durante la gravidanza e vengano applicate sistematicamente le linee guida a tutti i pazienti HIV positivi. Le madri provenienti dall'Europa centrale ed orientale ricoprono il 17.9% di questi casi. In data 21 marzo 2023, una donna di anni 22 alla 39+1 settimana di gestazione è giunta al pronto soccorso ostetico-ginecologico del nostro ospedale, dove è stata posta diagnosi di rottura prematura delle membrane e di condilomatosi vulvare florida. La paziente non ha riferito alcuna patologia o terapia cronica in atto. I test sierologici di screening hanno mostrato: pregressa infezione da CMV, EBV e T. gondii; negatività per virus epatitici, sifilide e rosolia. Il risultato del test per HIV, che mostrava positività per anticorpi e negatività per antigene p24, sono pervenuti durante il parto cesareo di emergenza: lo specialista di malattie infettive è stato convocato, ma non c'è stato tempo per la profilassi con zidovudina. La paziente era asintomatica, il suo numero di CD4+ era 140/µL (17%) con un rapporto CD4+/ CD8+ 0.3. Il test HIV-1 WB è risultato positivo in tutte le bande, mentre l'HIV-RNA plasmatico non è stato rilevabile. Dopo una settimana, utilizzando varie tecniche ed inviando campioni all'Ospedale Sacco, si è scoperto che la paziente aveva un'infezione da HIV-1 sottotipo A6 con HIV-RNA su plasma corrispondente a 98100 copie/mL e HIV-1 DNA su plasma di 19902 copie/106 cellule. Al pervenire della negatività di Cryptococcus-Ag e CMV-DNA su plasma, è stata introdotta la terapia antiretrovirale (TAF/ FTC/ BIC); il

Abstract

Despite HIV screening during pregnancy and guidelines applying to HIV-positive pregnant women, since the beginning of the epidemic to Dicember 31st 2022 in Italy were reported 742 vertically transmitted HIV pediatric cases; mothers from Central/Eastern Europe accounted for 17.9% of these cases.

On March 21th 2023, a 22-year-old Ukrainian at 39+1 weeks of gestation came to obstetric-gynecological ER of our Hospital; premature rupture of membranes (ROM) and vulvar condylomatosis were diagnosed. She didn't report any medical condition or therapy. Screening serological test showed: previous CMV, EBV and T. gondii infections; negativity for all hepatitis viruses, Syphilis and Rubella. Results of HIV test showing positive antibodies with negative p24-antigen became available whilst delivery via an emergency cesarean section was ongoing: the Infectious Diseases specialist was summoned, but no zidovudine prophylaxis could be timely administered.

She was asymptomatic, her CD4+ count was 140/µL (17%) with CD4+/CD8+ ratio 0.3. HIV-1 WB-assay was positive in all bands, while plasma HIV-RNA was undetectable. After a week, using various techniques and sending samples to Sacco Hospital, it was discovered HIV-1 subtype A6 infection with plasma HIV-RNA of 98100 copies/mL and HIV-1 DNA of 19902 copies/106 cells. Upon negative serum Cryptococcal-Ag and plasma CMV-DNA, she started antiretroviral therapy (TAF/FTC/BIC); treatment was well tolerated:

Corresponding Author:

Cinzia R. Bassoli
Infectious Diseases Unit, Legnano Hospital, ASST Ovest Milanese, Legnano, Italy

cinziaroberta.bassoli@asst-ovestmi.it

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trattamento è stato ben tollerato: dopo un mese, gli esami del sangue non hanno mostrato tossicità, il suo numero di CD4 + era di 150 cellule/µL e HIV-RNA su plasma è risultato non rilevabile.
La paziente ha partorito un neonato sano di sesso maschile, che ha iniziato immediatamente la PEP con zidovudina/lamivudina/nevirapina; il suo numero di CD4+ era di 1440 cellule/µL, il test HIV mostrava anticorpi positivi e antigene p24 negativo e l'HIV-RNA plasmatico era non rilevabile. Dopo una settimana, il neonato ha sviluppato un'eruzione eritemato-maculopapulare confluente sul tutto il soma, per cui la nevirapina è stata sostituita con lopinavir/ritonavir. È stato nutrito con latte artificiale, crescendo in maniera adeguata. Al pervenire di HIV-RNA e HIV-DNA su plasma non rilevabili in data 28 Marzo e il 12 Aprile si è decido di interrompere la profilassi post esposizione (PEP).
La nostra relazione evidenzia l'importanza dello screening sierologico pre-natale per l'HIV, specialmente nei soggetti vulnerabili provenienti da ambienti svantaggiati. È inaccettabile che la trasmissione verticale dell'infezione da HIV avvenga ancora oggi in Europa.
Fortunatamente, oggigiorno è infrequente dover gestire il caso di una donna che si scopre HIV-positiva al momento del travaglio, e speriamo che il nostro caso possa aiutare i giovani specialisti in malattie infettive in questo compito impegnativo e rischioso.

after one month, blood exams showed no toxicity, her CD4+ count was 150 cells/µL and plasma HIV-RNA was undetectable.
She gave birth to a healthy male newborn who started immediately PEP with zidovudine/lamivudine/nevirapine; CD4+ count was 1440 cells/µL, HIV-1 antibodies were positive, while HIV p24 Ag was negative and plasma HIV-RNA was undetectable. After one week, he developed a confluent erythematous-maculopapular rash over his body, so nevirapine was replaced with lopinavir/ritonavir. He was formula-fed, growing regularly.
Plasma HIV-RNA and HIV-DNA were still undetectable on March 28th and April 12th and post exposure prophylaxis (PEP) was discontinued.
Our case-report highlights the importance of pre-natal HIV testing, especially in vulnerable individuals coming from disadvantaged backgrounds. It is unacceptable that vertical transmission of HIV infection is nowadays still happening in Europe.
Fortunately, it is unfrequent these days to have to manage the case of a woman discovered HIV-positive during labour, and we hope our case could help younger Infectious Diseases specialists in this challenging and risky task.

Introduction

Despite successful HIV screening at first trimester, antiretroviral therapy in all people with HIV (PWH), pregnancy planning with Infectious Disease (ID) specialist and application of guidelines on antiretroviral therapy of HIV-positive pregnant women to reduce vertical transmission, in 2022 in Europe 270 new diagnoses of HIV were reported as being due to mother-to-child transmission during pregnancy, childbirth or breastfeeding. Most of the cases (220, 81.5%) were migrants born outside of the reporting country (1).
In Italy, since the beginning of the epidemic to December 31st, 2022, were reported 742 vertically transmitted HIV pediatric cases. Of these, 362 (48.8%) were from IDU mothers, while 278 (37.5%) from women who acquired HIV through sexual route. Foreign women represent 71.5% (587/821), coming mostly from Africa (74.1%), Central and Eastern Europe (17.9%), Latin America (5.6%) and Asia (2.4%) (2).
To ensure every woman is screened for HIV before pregnancy or at first trimester is crucial to prevent mother-to-child transmission and it is an opportunity for averting late diagnosis (defined as presenting for HIV care with a CD4+ count below 350/µL, or with an AIDS-defining event, regardless of the CD4+ cell count) with its poorer outcomes and increased risk of severe disease and death.

Purpose

Describing the case of a 22-year-old Ukrainian woman who came in Italy in March 2023 at 39 weeks of gestation to give birth to her first child. She was discovered HIV-positive during labour.

Description

In mid-March 2023 a 22-year-old Ukrainian woman at 38 weeks of her first gestation came alone to Northern Italy to give birth to her child because of the delicate politic situation in her Country that make it difficult to manage problems of the baby during pregnancy (probably fetus breech presentation, in this specific case).

On March 21st, 2023, at 39+1 weeks, she came to obstetric-gynecological ER of Legnano Hospital where was diagnosed premature rupture of membranes and florid vulvar condylomatosis. The patient did not report any medical condition or

chronic therapy, nor provided any documentation of the current pregnancy.
She was hospitalized for monitoring of maternal-fetal well-being and delivery assistance.
HIV Ag/Ab screening (VITROS HIV Combo, Ortho-Clinical Diagnostics and LIAISON XL Murex HIV Ab/Ag, DiaSorin) was performed during hospital stay as part of pregnancy routine screening. On March 21st the test came back positive (HIV-1 Ab positive, HIV p24 Ag negative), while the patient was already delivering the baby via emergency cesarean section. The ID consultant was alerted, but the timing did not allow peri- partum prophylaxis with zidovudine ev.
Other screening serological tests were performed and showed: previous CMV, EBV and T.gondii infections, negativity for HAV IgG, HBsAg, HBsAb, HBcAb, HCV Ab, T.pallidum Ab and Rubella IgG and IgM.
She was completely asymptomatic and her blood tests did not showed any abnormalities, apart from iron deficiency; her lymphocyte T subpopulations were CD4+ 140/µL 17%, CD8+ 560/µL 56%, CD4+/CD8+ ratio 0.3.
The mother was an orphan who grew up in an orphanage in Ukraine; at 20 years old, she got married with a man without known clinical conditions; she has been a housewife that lived in the countryside nearby Kiev, has never used injecting drugs and had sexual intercourse just with her husband.
HIV Ab test was confirmed with the positivity of HIV-1 western blot for p18, p24/25, p34, gp41, p40, p52, p55, p68, gp110/120 and gp160 (obtain with New Lav Blot 1, Bio-Rad on March 21st at Legnano Hospital) while HIV-RNA was undetectable (COBAS HIV-1 Test 4800 Roche on March 21st and repeated on March 22nd at Legnano Hospital; results were confermed at Sacco Hospital with samples collected on March 21st and on March 24th).
HIV-2 Ag/Ab test and HIV-2 western blot (New Lav Blot 2, Bio-Rad) were performed at our hospital and resulted indeterminate.
On March 31st other samples were sent to Sacco Hospital, and using various techniques (COBAS AmpliPrep, COBAS TaqMan HIV-1 Test V 2.0; HIV1 ELITe MGB by ELITechGroup; Xpert HIV-1 Viral Load by Cepheid) it was discovered she was infected with HIV-1 subtype A6 with plasma HIV-RNA of 98.100 cp/mL and HIV-1 DNA of 19.902 cp/106 cells. HIV resistance test carried out with 20% cut-off NGS showed K101Q and V179I mutation in RT, L101 and K20R in PR and L74I in INT. HLA-B*57:01 test was negative.
On April 5th, the results of plasma Cryptococcus Ag (negative) and plasma CMV-DNA quantitative PCR assay (negative) were received. Simultaneous HIV-RNA at Sacco Hospital was found to be 63.000 cp/mL. The same day the young woman started antiretroviral therapy with tenofovir alafenamide/emtricitabine/bictegravir.
The therapy was well tolerated and one month later her blood test did not showed any toxicities, while CD4+ lymphocyte count was 150 cells/µL (17%) and plasma HIV-RNA was undetectable with all the techniques performed.
She gave birth to a male newborn of 3100 g of weight (30° percentile) and 49 cm (25° percentile) of length and with APGAR score of 10/10, who started immediately post-exposure prophylaxis with triple antiretroviral therapy with zidovudine (12 mg bid), lamivudine (6 mg bid) and nevirapine (18 mg bid) according to guidelines.
The blood test of the baby at birth showed no abnormalities; his CD4+ lymphocyte count was 1440 cells/µL, HIV-1 Ab was positive, while HIV p24 Ag was negative and plasma HIV-RNA was undetectable. On March 28th a confluent erythematous maculopapular rash appeared over the whole body, so nevirapine was suspended and lopinavir/ritonavir was added. Therapy was then well tolerated, he has been fed with milk formula from birth, growing regularly, and his blood test just showed mild anemia (Hb 13.3 g/dL); every other routine check at birth (ECG, neonatal screening of congenital metabolic diseases, otoemissions, red reflex test, Ortolani maneuver, pulse oximetry and pre- and post-ductal perfusion index) was normal.
Plasma HIV-RNA and plasma HIV-DNA were repeated on March 28th and April 12th and were still undetectable, so it was decided to stop post-exposure prophylaxis.
Unfortunately, at the end of June 2023 they both moved from Legnano and were lost at follow-up.

Conclusions
add references for each statement

These case displays two main cause for thoughts: first of all, vertical transmission of HIV infection is nowadays still a strong impact problem in lots of Countries, but also in Italy. It is fundamental to pursue the implementation of screening programs

of pregnancy women to diagnose and treat timely, but it is also important to know how to manage particular cases, like the one here reported and to build a tailored therapy for each patient.
Diagnosis and treatment of this patient as well as the correct prophylaxis of her baby, lead to a successful management of two young lives despite the circumstances: a mother with a controlled HIV infection and a baby that, correctly prophylaxised, avoided being infected.
The correct management should be performed and granted to all the mothers that do not have the opportunity to check themselves during the pregnancy, to provide a timely diagnosis and an accurate therapeutic profile, personalized on the story and the clinical and laboratory features of the single patient and their children.

Secondly, Italy is a B subtype prevalent area, but the HIV-1 subtype geographic distribution is changing, with a consistent increase of non-B infections in regions where subtype B has been prevalent for a long time, such as in Western and Central Europe. This phenomenon is linked to migratory waves that imported them from other geographic locations. Subtype A6 is prevalent in Countries of the former Soviet Union, and collaboration between centres and use various techniques is fundamental to correctly identify HIV-1 subtype and range of viral load to better tailor therapy.
Fortunately, it is unfrequent these days to have to manage the case of a woman discovered HIV-positive during labour, and we hope our case could help younger Infectious Diseases specialists in this challenging and risky task. ■

REFERENCES

1. European Centre for Disease Prevention and Control. HIV/AIDS surveillance in Europe 2023 (2022 data). (last access May 27, 2024, at *https://www.ecdc.europa.eu/en/publications-data/hivaids-surveillance-europe-2023-2022-data*).
2. Istituto Superiore di Sanità. *Aggiornamento delle nuove diagnosi di infezione da HIV e dei casi di AIDS in Italia al 31 dicembre 2022.* Notiziario dell'ISS 2024; 36.