第15回日本エイズ学会

Interactive Session

症例から学ぶHIV感染症診療のコツ

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Case1 #1

33yo, married woman

- She was diagnosed HIV positive at week of 11
- No symptoms
- Concerning about risk of transmission to her baby
- CD4+ 616、HIV-RNA $<4.0 \times 10^2$
- You fully counseled about the risk of continuing pregnancy

Case1 #2

If she wants to continue pregnancy, which regimen will you recommend?

1. ZDV
2. NVP+ZDV+3TC
3. NFV+d4T+ddI
4. NFV+ZDV+3TC
5. No antiretrovirals

Case1 #3

When will you start her treatment?

1. Immediately
2. At week of 14th
3. At week of 24th
4. At week of 34th
5. One day prior to delivery

Case 1 (Cont.)

- She started ZDV at week of 14
- Elective C/S at week of 35
- ZDV prophylaxsis to the infant
- One year later: CD4 658、HIV-RNA $<4.0 \times 10^2$
- Baby is HIV-RNA negative, and growing normaly

Case2 #1

27 yo married women

- In 1997, she was diagnosed HIV(＋)in perinatal care
- She delivered her baby without HIV management,

  But her baby was not infected with HIV.
- In 1999 ,She came to your clinic and showing thrombocytopenia

  (October)CD4: 300　HIV-RNA : 2.5×10^5　Plt:60,000
- No subjective symptom

Case2 #2

She is concerning her next baby.
Which regimen will you recommend?

1. EFV+ZDV+3TC
2. NFV+ZDV+3TC
3. EFV+d4T+ddI
4. NVP+ZDV+3TC
5. ZDV

Case2 #3

Case2（Cont.）

- She started HAART with NFV+ZDV+3TC
- 3 month later　CD4:412　HIV-RNA: <50 copies
- 6 month later　switched ZDV to d4T because she developed anemia
- 12 month later　CD4:648　HIV-RNA: <50 copies
- 18 month later　She found herself pregnant. Plt:180,000

Case2 #4

Which treatment plan will you recommend?

1. Stop HAART till week of 14th , then come back on same regimen after 14th week
2. Stop HAART till week of 14th , start her treatment again with ZDV
3. Stop HAART, and start her treatment again after delivery
4. Continue HAART
5. Continue HAART , and change d4T to ZDV

Case2 #5

Case2 （Cont.）

- She continued HAART with same regimen(d4T+3TC+NFV)
- At the week of 32, CD4: 600 HIV-RNA: <50 copies
- She delivered her baby without complication.
- 3 month later CD4: 758、HIV-RNA: <50 copies
- Her baby's HIV-RNA is negative, and growing normally

Case3 #1

S.O. is a 30 year-old G_6 P_3 A_2. She was diagnosed HIV+ in 1991. One of her three children died at one year of age.
The other two are healthy. She is highly antiretrovirally exposed, with a history of:

1993	ZDV for 2 months and d4T, ZDV, ddI for 1 month
1998	NVP, 3TC, IDV for two months
1999	ZDV, 3TC, EFV (12 June - 14 July)

Case3 #2

Recent laboratory values for S.O. are:

Date (1999)	CD4 (cells/μl)	pl HIV RNA (copies/ml)
16 July	Positive Urine Pregnancy Test	
	211	100,000
12 August	73	111,834
19 August	Resistance testing shows resistance to all nnRTIs.	
8 September	116	206,519

Case3 #3

You first meet S.O. in your office on 12 August. She has taken no antiretrovirals since discovering she was pregnant in July. She is feeling well. She thinks she is about "three months" pregnant. On this first visit, you would:

1. Advise immediate termination of pregnancy because of efavirenz exposure.
2. Ascertain whether this is a desired pregnancy.
3. Restart combination antiretroviral therapy immediately.
4. Start zidovudine alone to prevent vertical transmission.
5. Resolve never to prescribe efavirenz to any woman of reproductive age.

Case3 #4

S.O. relates that this was not a planned pregnancy, but is very much desired, and that she does not want an abortion "no matter what." Your next step in providing care for her is to:

1. Advise her of the risks of neural tube defects in monkey studies following in utero efavirenz exposure.
2. Obtain an obstetrical ultrasound to determine fetal gestational age.
3. Tell patient you cannot care for her because of the risk that you might be held responsible for the birth of a deformed baby.
4. Start zidovudine monotherapy immediately.
5. Obtain resistance testing.

Notes for case 3 #4

- Neural tube defects (and most congenital anomalies) occur well before 11 weeks gestation.
- S.O. cannot be advised of the risk to her baby if you do not know her gestational age.
- Similarly, recommendations regarding antiretrovirals cannot be made until the gestational age is known.

Case3 #6

If you document first trimester fetal efavirenz exposure, reassuring data can be obtained from which of the following:

1. Ultrasound as early as 10 weeks gestational age.
2. Maternal blood tests at 16-20 weeks gestational age.
3. Ultrasound at 18-22 weeks gestational age.
4. All of the above.

Notes for case 3 #6:

- Obstetrical ultrasound can often rule out anencepahly as early as 10 weeks gestation.
- Maternal serum alpha fetal protein (MSAFP) is a marker for open fetal neural tube and abdominal wall defects. A value >2MOM is not diagnostic, but a normal value would be very reassuring.
- Ultrasound at18–22 weeks is highly sensitive at detecting neural tube defects and many other congenital anomalies.

Case3 #8

After her third visit (8 September) to your office, at 16 weeks gestational age, you become concerned about S.O.'s high viral load and low CD4 count. You offer:

1. ZDV monotherapy because it is the only thing proven safe in pregnancy.
2. A one-pill ZDV/3TC combination because it is easy for this non-compliant individual to take.
3. A four-drug combination aimed at maximal potency for control of maternal plasma viremia.
4. ZDV/3TC combination plus NVP for ease of administration and benefits of triple combination therapy.
5. No therapy or prophylaxis now, because mother is not sick, and baby will probably not survive anyway, due to the efavirenz exposure.

Case3 #9

Recent laboratory values for S.O. are:

Date (1999)	CD4 (cells/μl)	pl HIV RNA (copies/ml)
16 July	Positive Urine Pregnancy Test	
	211	100,000
12 August	73	111,834
19 August	Resistance testing shows resistance to all nnRTIs.	
8 September	116	206,519

Case3 #10

Notes for case 3 #8

- Pregnant women should receive access to HIV therapy regardless of their reproductive status.
- By any standard, SO has AIDS and a high chance of dying in the next five years. She should be offered potent therapy aimed and durable suppression of viral replication.
- Neither ZDV monotherapy nor Combivir alone are potent enough to control SO's high viral load.
- Given her history, there is a high likelihood that she may be resistant to ZDV, 3TC and NVP.
- NVP is not the best choice for someone who has had major adherence problems in the past.

Case3 #11

Which of the following options would you offer this mother?

1. Switch to a "megaHAART" regimen that includes efavirenz and hydroxyurea.
2. Discontinue all medications and begin ZDV monotherpay per ACTG 076 guidelines.
3. Complete switch to d4T/ABC/RTV/IDV.
4. Nothing. Counsel patient and her husband that there is now little to do to prevent transmission of a highly resistant virus to their baby.
5. Return to most recent combination. Counsel patient and her husband that the baby is likely to be born with birth defects if she decides to take efavirenz

Notes for case 3 #11

- While hydroxyurea has been used safely in pregnancy for treatment of sickle cell anemia, there are many other options to this.
- SO is efavirenz-experienced and non-adherent, therefore very likely nnRTI resistant.
- While there are other reasonable combinations, this one offered highly potent agents with a complete switch.
- Even though unlikely to be effective, efavirenz would not induce birth defects at this gestational age.
- SO's infant was uninfected.

Case4 #1

C.M. is a 34 year-old, Gravida 3, Para 1 at 30 weeks of pregnancy. She has taken combination antiretroviral therapy since 1996. One year ago her viral load was 1,665, CD4 529. She is very adherent to therapy. Current data:

Viral load	33,525 copies/ml
CD4	229 cells/μl

Genotypic resistance to:

- all NRTI
- NVP
- all available PIs

Case4 #2

CM's current regimen is ABC, NVP, RTV (200 mg) and IDV (800 mg) all twice daily. Which of the following options would you offer this mother?

1. Switch to a "megaHAART" regimen that includes efavirenz and hydroxyurea.
2. Discontinue all medications and begin ZDValone per ACTG 076 guidelines.
3. Empiric switch to d4T/ddI/RTV/IDV.
4. Counsel patient and her husband that there is now little to do to prevent transmission of a highly resistant virus to their baby.
5. Counsel patient and her husband that the baby is likely to be born with birth defects if she decides to take efavirenz

Notes for case 4 #2

- At this point, there are many more highly potent options available. While hydroxyurea has been safely used in pregnancy for sickle cell anemia, we have no experience in the setting of HIV. NVP resistance suggests EFV resistance.
- ZDV alone offers doubtful benefit to mother and baby in this setting of documented clinical and genotypic resistance.
- The d4T/ddI combination has resulted in a handful of case reports of lactic acidosis in pregnant women.
- To date there is only one case report of vertical transmission of resistant virus.
- Efavirenz started at 30 weeks of pregnancy will not cause neural tube defects.

Case4 #4

You discover that C.M. had self-adjusted her ritonavir dosage to 100 mg twice daily. Still, she has decided to try a "switch" to twice-daily d4T/ddI/RTV200/IDV800. Over the next month her viral burden falls to 3,452 copies/ml. C.M. has requested an elective cesarean section at 37 4/7 weeks.

Six days before delivery, phenotypic testing results return, showing high resistance to ZDV and NVP and high sensitivity to efavirenz.

Case4 #5

Which of the following delivery plans offered to C.M. do you think is the worst?

1. Continue all medications. Add IV ZDV one day prior to delivery. Administer ZDV prophylaxis to the infant until six weeks of age.
2. Continue all medications. Add EFV, 3TC, IV ZDV one day prior to delivery. Administer ZDV prophylaxsis to the infant until six weeks of age.
3. Continue all medications. Add IV ZDV one day prior to delivery. Administer ZDV and NVP prophylaxis to the infant until six weeks of age.
4. Stop all medications one day prior to delivery and start IV ZDV. Administer ZDV prophylaxis to the infant until six weeks of age.
5. Continue all medications. Add EFV, 3TC, IV ZDV one day prior to delivery. Administer d4T, ddI, NVP prophylaxis to the infant.

Case4 #6

Based on this information the following delivery plans were offered to C.M. Which do you believe is the best?

1. Continue all medications. Add IV ZDV one day prior to delivery. Administer ZDV prophylaxis to the infant until six weeks of age.
2. Continue all medications. Add EFV, 3TC, IV ZDV one day prior to delivery. Administer ZDV prophylaxsis to the infant until six weeks of age.
3. Continue all medications. Add IV ZDV one day prior to delivery. Administer ZDV and NVP prophylaxis to the infant until six weeks of age.
4. Stop all medications one day prior to delivery and start IV ZDV. Administer ZDV prophylaxis to the infant until six weeks of age.
5. Continue all medications. Add EFV, 3TC, IV ZDV one day prior to delivery. Administer d4T, ddI, NVP prophylaxis to the infant.

Notes for case 4 #5 and #6:

- There are no right answers to these questions.
- Guidelines do not yet exist to help us decide whether ZDV prophylaxis is effective when there is clear evidence of high level maternal clinical, genotypic and phenotypic ADV resistance.
- In San Francisco, we have found it helpful to separate issues of maternal health from issues of perinatal transmission prophylaxis when identifying options.
- CM chose option 5, adding EFV, 3TC and IV ZDV one day before delivery by elective cesarean section. She requested that her infant be placed on d4T, ddI and NVP for prophylaxis.

Notes for case 4 #5 and #6:

- CM is an unusual case of advanced HIV disease and resistance to all available medications. She requested "everything possible" that could be done to prevent transmission to her infant.
- There is no justification for jeopardizing maternal viral control by stopping medications here.
- We reasoned that the addition of 3 medications that CM had not taken for some time could be of benefit. The fetus was given triple prophylaxis because of mother's resistance profile.

Case4 #9

Notes for case 4 #5 and #6:

- C.M. delivered a healthy 2850 g girl by elective cesarean section as planned.
- Today, eighteen months later, C.M. is feeling well, and is happy with her two children after recovering from a serious post-partum depression. She has mild symptoms of lipodystrophy.
- Most recent laboratory values:

Mother:	VL	<50 copies/ml
	CD4	517 cells/µl
Baby:	HIV-1 DNA PCR	negative x 4
	HIV-1 antibody	negative at 16 months

Case5 #1

M.B., a 30 year old Gravida 5 Para 1 is referred to you after testing HIV+ on prenatal screening. She denies any risk factors except for unprotected vaginal intercourse. She is 15 weeks pregnant and complains of a vaginal discharge.
Over the next month, you attempt to treat her bacterial vaginosis first with metronidazole, then with clindamycin, but she refuses to take the medication and states she does not like "putting unnatural chemicals" in her body and that she hates taking pills.

Case5 #2

By 22 weeks gestation you are becoming concerned about her ability to take antiretroviral therapy during pregnancy. Her CD4 =492 and VL=2,490. She refuses to take more than one pill to prevent transmission to her baby, and wants no therapy for her health. Which option do you think is safest for her and the fetus?

1. Late second trimester abortion .
2. One Combivir (ZDV/3TC) capsule twice daily.
3. Combivir + nevirapine twice daily.
4. Nevirapine alone.
5. ZDV 300mg twice daily.

Case5 #3

Notes for case 5 #2:

- Reproductive choice involves self-determination. While M.B. requires education regarding HIV disease and pregnancy, it is not appropriate to *recommend* either continuation or termination of the pregnancy at any time.
- Combivir alone is outside of standard of care for all individuals and is highly likely to rapidly induce nRTI resistance, which can be vertically transmitted.
- Combivir/nevirapine is a reasonable choice, however skipped doses will lead rapidly to nnRTI resistance. It is pointless to insist on a regimen that a woman has already told you she does not want take.


Combivir
Alone

Case5 #4

Notes for case 5 #2:

- The risk of transmission at this viral burden is low (<5%) and probably lower still with ZDV prophylaxis. ZDV alone is low potency, and may not induce resistance in the short time it is given.
- This mother will require intensive case management after baby is born, with support an education regarding infant nutrition, testing and ZDV prophylaxis.
- We have found that giving women the power to make important treatment decisions helps them become invested in their own treatment or prophylaxis strategies. It improves communication and adherence. If caregivers insist on treatments a patient does not want, she will simply agree to one thing and do another.