National Clinical Symposium
Drug Toxicity Workshop

September 14 -15, 2006

NCHADS Social Health Clinic

Case Study

Case study – drug toxicity

- 34 year-old woman, diagnosed HIV +ve January 2006

- Minimal symptoms
- Past medical history:
  - No previousTB
  - No previous OI Prophylaxis
  - No ARV experience
  - No traditional Khmer/Chinese medicine
- No history of drug allergy

Exam:

- Weight 45 Kg
- WHO stage III (oral thrush), no evidence of active OI

- Commenced OI prophylaxis: cotrimoxazole and fluconazole

- Laboratory results at baseline
  - CD4: 78 cells / µL
  - Hb: 111g/L
  - LFT: AST = 99 U/L, ALT = 94 U/L
  - HBV sAg negative
  - HCV Ab negative
  - CXR normal

- Commenced ARV (35 days after start OI prophylaxis)
  - D4T 30mg + 3TC + NVP (lead in dose for 14 days)
- Follow up day 14 after start ARV

  History:
  - 4 days mild itchy rash on both arms
  - 7 days of nausea occasional vomiting, no fever, no shortness of breath.

  Exam:
  - afebrile, VS normal
  - mild maculo-papular rash on both arms
  - other exam unremarkable

- Results of routine Lab monitoring at 2 weeks after start ARV
  - AST = 51U/L, ALT = 57 U/L
- What is the cause of skin rash?
  - NVP?
  - Cotrimoxazole?
- What is your management plan?
  - stop all ARV? stop NVP only? stop cotrim only? continue cotrim + ARV but keep NVP lead in dose and closely observe? continue cotrim and increase NVP to full dose?

- Our Management
  - continued ARV with NVP lead in dose for 3 more days, kept OI prophylaxis and prescribed antihistamine.
  - planned follow up in 3 days

- Three days later
  - skin rash and nausea had resolved
  - switched to full dose NVP

- Plan
  - follow up + check routine LFT in 2 weeks (after NVP full dose).
  - explained patient to come early or call doctor if any symptoms.

- Patient came 2 days prior to planned follow up (28 days of ART)

History

- 3 days recurrence of itchy skin rash on both arms, back and abdomen + symptoms of fever

Examination

- afebrile, VS normal
- moderate dry, patchy maculo-papular rash on arms, back and abdomen. No mucus membrane involvement.

- What is the most likely cause of skin rash?
  - NVP?
  - Cotrimoxazole?
  - Other?

- What is your management plan?
  - Stop all ARV?
  - Stop all ARV and cotrim?
  - Stop NVP and continue D4T, 3TC for 10 days?
  - Stop cotrim and continue same ARV?

- Our Management:
  - ceased cotrimoxazole
  - continued same ARV
  - gave antihistamine and Calamine skin lotion
  - Checked liver function
  - follow up planned in 3 days
  - explained patient to come early or call doctor if any symptoms.

- Follow up at 3 days (~31 days ART)

  History:
  - Skin rash worst , noticed mild redness both eyes
  - Fever with chill once daily
  - Sore throat when swallow, mild abdominal pain on epigastric area

  Examination:
  - T 38^0C, other VS normal
  - mild conjunctival redness both eyes
  - dry lips, mildly red pharynx and tonsils, no mouth ulceration
  - skin rash worse, generalized over body, dry, no blisters
  - abdomen: soft mildly tender liver palpated 2 cm below costal margin

  LFT : AST 144U/L, ALT = 202 U/L

Skin rash day 31 post commencement of ART

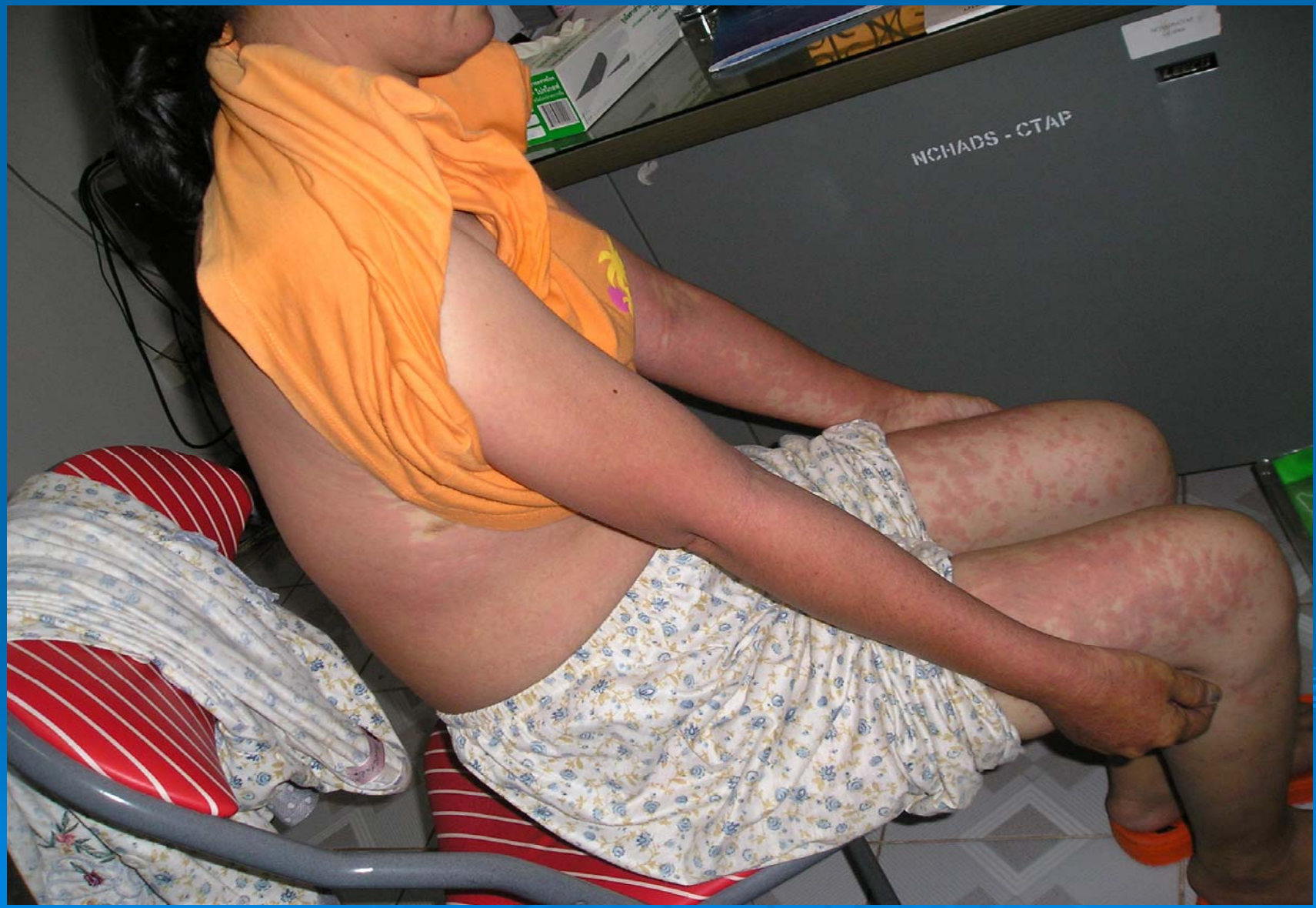

Photo presented with the patient's consent

What is your management plan now?

- Stop all ARV ?
- Stop NVP only and continue D4T, 3TC for 10 days ?
- Stop NVP and switch immediately to EFV?
- Stop NVP and switch immediately start PI?
- Stop fluconazole ?

- Our Management:
  - ceased fluconazole
  - ceased NVP and continued D4T+3TC for 10 days
  - planned to restart with EFV when the rash completely resolve and liver function significantly improved
  - follow up at 3 days then weekly
- 24 days after stop NVP
  - skin rash resolved and liver function normal
  - commenced D4T 30 mg + 3TC + EFV
- One month after recommenced ART
  - asymptomatic, LFT normal
  - recommenced fluconazole + cotrimoxazole
- No recurrence of rash or abnormal LFT

National Guidelines for the use of antiretroviral therapy in adults and adolescents (2003)

Table 8: Changing ARV because of side effects (see p18 for side effect management)

NVP	Rash – moderate to severe (eg bullae, "wet")	Change NVP to EFV	Never use NVP again
	Rash – complicated (mucosal involvement or fever)	Change NVP to PI or ABC	Never use NVP or EFV again
	Hepatitis	Change NVP to EFV	Never use NVP again
	Hepatitis – severe or life threatening	Change NVP to PI or ABC	Never use NVP or EFV again

Moderate dry rash with fever – should the guidelines be reconsidered and clarified ???


Thank yoy very much