ABSTRACT

Although HIV is a chronic disease, there are several clinical conditions associated with it, which can trigger life threatening emergencies. The target organs may involve cardiopulmonary, neurologic, gastrointestinal, haematologic and renal systems. Microbiologic confirmation in certain life threatening infections is limited by availability of rapid and reliable tests.

Several issues pertaining to the patients’ current antiretroviral therapy, potential drug interactions and immune reconstitution inflammatory syndrome etc remains a major challenge. Besides, many non-infectious entities (including rapidly spreading malignancies) distinct to HIV per se are being increasingly recognized. An additional challenge in resource poor settings is the need to observe universal workplace precautions at all times and round the clock availability of drugs for post exposure prophylaxis.

INTRODUCTION

Although HIV is being increasingly recognized as a “chronic manageable disease”, there are several situations when a HIV / AIDS patient requires care in the ‘intensive care unit’ (ICU). In this context, most admissions are due to ‘life threatening opportunistic infections’ (OIs). However, as more and more patients are being put on antiretroviral treatment (ART), few additional indications for admissions to ICU are emerging such as:

1. ART related drug toxicity
2. Severe ‘immune reconstitution syndrome’ (IRIS)
3. HIV related organ dysfunction:- eg: HIV cardiomyopathy, HIV cholangiopathy, HIV nephropathy.
4. HIV related oncologic emergencies
5. HIV unrelated emergencies: Acute myocardial infarction, poisonings, substance abuse related toxicity, road traffic accidents etc.

Two distinct subset of patients have emerged:

A. Those on ART and full access to care: These patients live longer, are sexually active longer, have decreasing incidence of OIs and likely to require ICU admission for ‘non-HIV related’ emergencies.

B. Those NOT on ART and with minimal / no access to care: These patients are likely to require ICU admission for life threatening OIs. Quite a few are not even aware of their

Fig. 1 : Principal Diagnosis Received by Patients with HIV on Admission to the Medical or Surgical ICU at San Francisco General Hospital between 1981 and 2003.

The principal diagnosis on admission to the ICU is reported for 86 patients from March 1981 to December 1985, followed by a gap of six years; then for 443 patients (an average of 111 patients per year) from January 1992 to December 1995, for 354 patients (an average of 88 patients per year) from January 1996 to December 1999, and for 328 patients (an average of 82 patients per year) from January 2000 to December 2003.

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‘positive’ status OR may willfully suppress their HIV status.

However, survival for patients with HIV admitted to the ICU continues to improve in the current era of combination ART. (1).

The ICU physician is faced with certain unique management issues:

- To continue or discontinue previous ART
- Unique drug-drug interactions
- Altered pharmacodynamics / kinetics of antiretroviral medication (as patient may be on nasogastric tube and certain medications cannot be crushed)
- Staff to be sensitized for observing ‘universal precautions’ at all times.
- Ensure 24x7 availability of medication for ‘post-exposure prophylaxis’.
- Close liaison with the diagnostic laboratory staff for early confirmation of the infectious agent causing the life threatening OI.

Pitfalls in the laboratory diagnosis may include:

- Patient too sick to provide specimen: eg sputum
- Patient is hemodynamically unstable for invasive procedures such bronchoscopy, CSF examination etc.
- Non-availability of support lab staff to perform specific lab tests round-the-clock.
- Low yield (sensitivity) for culture isolation in various body fluids.
- Delayed confirmation (eg: serology, culture isolation).

Due to the above factors, the ICU physician has to make an “early clinical diagnosis”. Some clinical clues include:

- The latest CD4 count: (and not the past nadir values)
- At any given CD4 count, the patient with higher viral load is at greater risk for an OI.
- Those with a past history of OI are at higher risk for subsequent OIs.
- In advanced stages (CD4 < 50), more than one OI can co-exist.
- Always analyze ‘new’ symptoms in the following light:
  a. Is it due to an OI?
  b. Is it due to side effect / toxicity of the ART
  c. Is it an IRIS?
  d. Is it unrelated to the HIV per se?
  e. Is it due to an HIV related malignancy?

CARDIO-PULMONARY EMERGENCIES

- Constitute one of the most important causes for an ICU admission.
- There is an increasing trend in mortality and antibiotic resistance in ‘invasive pneumococcal disease’, which is still one of the most common cause of community acquired pneumonia.(2).
- Hypoxia may be life threatening (especially in case of pneumocystis pneumonia) and may require mechanical ventilation. The initial X-ray chest may be normal.
- As high dose of co-trimoxazole is used, the ICU physician must monitor for side effects such as hyperkalemia, neutropenia, acute folate deficiency.
- TB also may present acutely especially as a massive pleural effusion or pericardial effusion (leading to cardiac tamponade).
- Microbiological confirmation is difficult due to inability to collect a representative sputum sample (patient too sick to expectorate) and limitations in getting a fiberoptic bronchoscopy for a bronchioalveolar lavage fluid.

ALWAYS REMEMBER THE POSSIBILITY OF CO-INFECTIONS

especially at low CD4 counts (for eg: PCP + miliary TB), if the initial response to the primary infection is not seen.

- IRIS is not uncommon especially when the CD4 is < 100 and the viral load > 100,000 copies /ml and patient is on ART, and should be considered in the differential diagnosis in a known patient on recent anti-TB medication. The above clinical condition may require the use of corticosteroids.
- Pericardial tamponade (due to TB, rarely malignancy) can present with acute onset shortness of breath and hypotension, requiring life-saving pericardiocentesis.
• There are increasing reports of acute myocardial infarctions, especially due to hypertriglyceridemia and hyperglycemia. Also, increased incidence of stent re-stenosis has been reported in these patients.

• HIV cardiomyopathy is a distinct clinical entity, and can present acutely with features of biventricular failure. 2D-echo done as an emergency bedside procedure can clinch the diagnosis.

• Acute pulmonary thromboembolism (due to HIV associated pulmonary vasculitis) though relatively rare is an important medical emergency and requires CT pulmonary angiography and subsequent anticoagulation / lytic therapy.

• **REMEMBER**: Drugs like stavudine, didinosine etc can precipitate life-threatening lactic acidosis and patients may present to the ICU as ‘acute onset shortness of breath’.

**RENAL EMERGENCIES**

• Acute gastroenteritis is not uncommon and may lead to acute tubular necrosis.

• HIV associated nephropathy (HIVAN) may rarely present like a ‘rapidly progressively glomerulonephritis’ (RPGN) requiring dialysis support.

• “Indinavir crystalluria” can present as acute ureteric colic.

• The nature of dialysis is an important issue as most centers do not have a dedicated hemodialysis machine. Continuous cycled peritoneal dialysis is one of the options.

• In the Indian scenario, the nephrotoxic effects of ‘native treatment’ and other self-medication(s) should always be considered.

**NEUROLOGIC EMERGENCIES:**

• HIV can involve any part of the neuroaxis acutely at any stage of the disease.

• Typically TB can present with complications of hydrocephalus (requiring emergency ‘shunt surgery’), abscess (requiring drainage).

• Others include toxoplasmosis which presents with acute onset focal deficit and/or seizures. However, seizure threshold may be significantly reduced with concomitant use of quinolones, efavirenz, INH etc.

• Headache of recent onset should always prompt a CSF examination. Cryptococcal meningitis can present without any fever and frank signs of meningeal irritation.

• It is preferable to precede a CSF examination by a CT scan. A contrast study should always be done (unless there are absolute contraindications).

• Non-infectious neuro emergencies include lymphoma, AIDP, pyomyositis.

**“ACUTE CYTOPENIAS”**

• Acute progressive anemia: may be due to Zidovudine.

• Some can present as acute ‘megaloblastic crisis’ due to folate / B12 deficiency as high output cardiac failure.

• Acute leucopenia: Stavudine is an important drug in the check list. Viral infections such CMV and EBV can be important causes.

• Acute thrombocytopenia leading to life threatening bleeding can be due to ‘immune thrombocytopenia’ due to HIV per se. Others include drugs such as sulphas, quinine etc.

• “Acute pancytopenia” is another hematologic emergency with varied aetiological factors such as infections, drugs, nutritional factors.

• All of the above conditions require an emergency ‘bone marrow aspiration’ / trephine biopsy and appropriate cultures/ staining (including salmonella, malaria, TB, Histoplasmosis, CMV etc).

What should the intensivist know about ‘anti-retroviral drugs’?

A. Most anti-retroviral drugs are available in oral formulations, and hence unpredictable pharmacokinetics.

B. Crushing some of the tablets (for the purpose of administering through the naso-gastric tube) can alter the drug release properties of certain ‘sustained release’ preparations.

C. Few days of discontinuation of antiretroviral drugs can result in emergence of resistance.

D. In case of suspected drug toxicity, it is difficult to attribute to a particular drug.

E. Likewise, if the ART needs to be discontinued, those with longer half lives (eg: nevirapine) have to be discontinued first).

F. Initiating antiretroviral therapy for the first time in the ICU (especially in patients with concomitant Anti-TB treatment) can trigger a severe ‘immune reconstitution inflammatory syndrome’.

G. However, initiating anti-retroviral therapy is ‘not’ a medical emergency.

**COMMON / IMPORTANT DRUG-DRUG INTERACTIONS**

**Drug requiring dose adjustment in patients with renal insufficiency†**

All NRTIs except for abacavir (Ziagen)

**Drugs requiring dose adjustment in patients with hepatic impairment‡**
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Atazanavir (Reyataz), fosamprenavir (Lexiva), and indinavir (Crixivan)

Common ICU drugs contraindicated with NNRTIs
Midazolam and triazolam (both with efavirenz)

Common ICU drugs contraindicated with protease inhibitors
Midazolam, triazolam, amiodarone (with indinavir, ritonavir, or tipranavir), bepridil (with atazanavir, fosamprenavir, ritonavir, or tipranavir), proton-pump inhibitors (with atazanavir), histamine blockers (if doses are administered twice daily with atazanavir), propafenone (with lopinavir and ritonavir, ritonavir monotherapy, or tipranavir), and quinidine (with ritonavir or tipranavir)

HIV AND THE HEALTH CAREWORKER
The intensivist taking care of the HIV positive patient is expected to observe "Universal work place" precautions at all times (irrespective of the status of the patient). This includes the use of protective gloves, mask, eye goggles etc. Also, similar precautions are necessary to be observed while performing bedside procedures.

It is also essential to make medication recommended for ‘post-exposure prophylaxis’ available accessible to the health care at all times, as ICU is a risk area for occupational exposure.

SUMMARY
HIV-related emergencies pose a great challenge to the intensivist. Although, most admissions are due to life-threatening opportunistic infections, of late HIV unrelated emergencies such as acute myocardial infarction, poisonings, substance abuse and drug toxicities are increasingly on the rise. The intensivist should ensure universal work place precautions at all times in the ICU.

REFERENCES