Case Report

AIDS And Its Complications. A Case Report And Review Of The Subject

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Abstract: Infection with HIV causes a spectrum of clinical problems beginning at the time of seroconversion (primary HIV) and terminating with full blown Acquired Immune deficiency Syndrome (AIDS) and death. This article describes the case of a 45-year-old gentleman who presented with 2 months history of fever and weight loss. He was diagnosed as a case of HIV on Elisa testing. He had extremely low CD 4 count and was suffering from opportunistic infections like Pneumocystis Carinii Pneumonia (PCP). The literature is reviewed on AIDS with a special focus on recent advances and highly active antiretroviral therapy.

Keywords: HIV, AIDS, PCP

Introduction

A 38 year-old gentleman of foreign nationality was admitted in hospital through Accident and emergency department with a history of drowsiness for last 3 days. Detailed history was taken from attendants. Patient had complaints of feeling unwell, malaise, non productive cough for the last 10 days, which was preceded by history of low-grade fever, loss of appetite, and generalised weakness for the last 2 months. He was a chain smoker and had significant history of alcohol intake. There was no history of drug addiction. He was a businessman by profession and used to travel abroad to different countries and had frequent sexual relations with prostitutes. He was divorced with one daughter who was not living with him either His father was a diabetic and hypertensive. Other members of his family were healthy.

On examination, the patient was markedly emaciated, and was in altered state of consciousness with a GCS of 8/15. He had marked pallor and clubbing. He had bilateral palmer erythema probably due to alcohol abuse and liver involvement secondary to it. Left anterior and posterior cervical chains of lymph nodes were palpable. He had also developed a bed sore at sacral area. He also looked dehydrated and was so weak that he had to be moved with assistance. His pulse rate was 110/min, regular and low volume and blood pressure was 100/70 without postural drop. He was afebrile on admission.

He had signs of meningeal irritation, increased tone in all limbs, normal reflexes and non-specific plantars. Power was 2/5 in all limbs. Sensory system could not be assessed due to patient's altered state of consciousness. There were bilateral coarse crepitations in basal areas of lungs.

Table-1: Initial basic investigations were as follows.

Investigations	Results
Hb	8.9 g/dl
Platelets	$73x10^9$ /IL
PT (Control 13.0)	14.0 Sec
APTT (Control 30.0)	45.0 Sec
TLC	$2.2x10^9$ /IL
ESR	90 mm in 1st hr
Polymorphs	85 %
Lymphocytes	95 %
Monocytes	03 %
Eosinophils	02 %
Bands	05 %
Bands	25,000

Peripheral blood picture showed anisopoikilocytosis, macrocytosis, acanthocytes, fragmented cells, elliptocytes and spherocytes. Malarial Parasites were not found on slides. Urine, stool and blood culture and sensitivity did not show any growth of organisms. Renal function tests and LFTs were normal initially. Among electrolytes, sodium was 128 mmol/ L, calcium 6.7mg/dl with albumin of 2.0g/dl. Serum ammonia was 253.

In view of his drowsiness and neck rigidity CSF examination was carried out which showed that glucose was low and proteins were high. Blood sugar level was 130 mg/dl. TLC was 03/cmm with 100 %

were all negative.

Hepatitis B and C serology, dengue IgG and IgM were all negative; however HIV 1&2 antibody test by Elisa was repeatedly strongly positive from two different laboratories. Cytomegalovirus IgG and IgM were also positive.

Chest X- Ray showed infective patchy and nodular infiltrates in both lungs together with right paratracheal lymphadenopathy **(See Figure-A).** Ultrasound abdomen showed peri-portal and coeliac lymphadenopathy. MRI Brain with contrast showed mild to moderate dilatation of ventricular system and a tiny remote infarct in posterior limb of internal capsule. **(See Figure- B)**

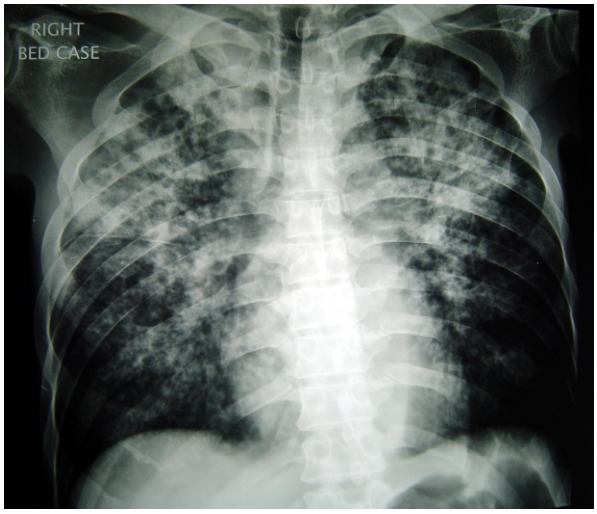

Figure-A: X-Ray chest.

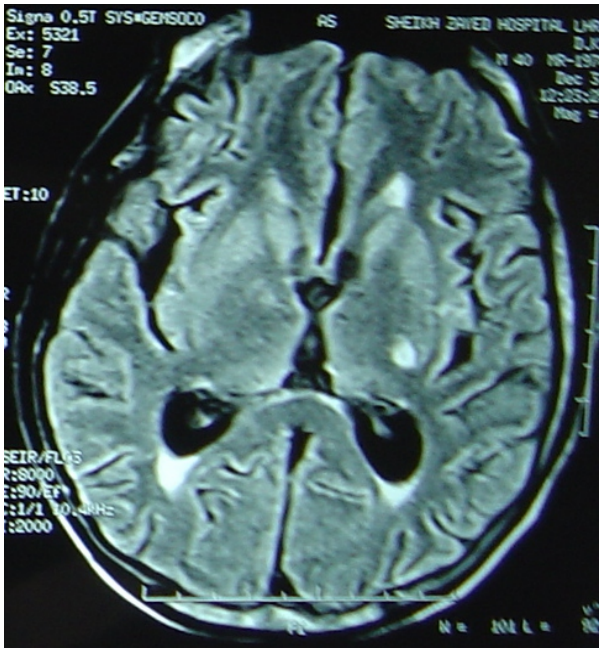

Figure-B: CT scan brain.

Firstly, it was thought that this patient might have pulmonary tuberculosis perhaps with tuberculous meningitis, explained by raised ESR, low sodium, high protein and low glucose in CSF. Therefore he was started on anti tuberculous therapy, keeping an eye on LFTs and other parameters. He was also started on high dose co-trimoxazole, thinking strong possibility of Pneumocystis carinii pneumonia. He was also given broad spectrum antibiotics parenterally along with gancyclovir for cytomegalovirus infection. Other treatment was mainly supportive in the form of blood transfusion, intravenous fluids, multi vitamins, intravenous albumin and parenteral nutrition. Bed sore was treated with daily washing it with normal saline, dressing and postural changes. Initially there was mild improvement but then patient's consciousness level fluctuated during the course of treatment with spikes of fever and his total leucocytes count continued to drop.

His repeat chest X-rays did not show any resolution of Pneumocystis carinii pneumonia inspite of treatment. Patient's general condition deteriorated. He went into deep coma and expired about 3 weeks after admission. The final diagnosis was a full blown Immunod- eficiency syndrome with all its recognisable complications except Kaposi Sarcoma i.e. Pneumocystis carinii pneumonia and Cytomegalovirus infection. Although he was given whatever treatment was available but he could not be given highly active antiretroviral therapy due to lack of facilities and a specialised unit. He could not be transferred to his own country, which had facilities, due to his very critical condition and extremely low CD4 count.

Here is a review of the literature about current concepts related to AIDS.

Literature Review

Human immunodeficiency virus (HIV) is a retrovirus that can lead to Acquired Immune Deficiency Syndrome (AIDS), a condition in which the immune system begins to fail, rapidly leading to life-threatening complications.[1] Epidemiology of AIDS is sown in the following table (Table 1) [2] in a simplified way. In Pakistan HIV prevalence rates among intravenous drug abusers ranged between 10 to 50 percent in and around Quetta, Faisalabad, Hyderabad, Karachi, and Sargodha. Surveillance data for 2006 point to a local concentrated epidemic among male sex workers and transgenders in Larkana and Karachi in the Sindh province while prevalence elsewhere is still below 5 percent.[3]

Table-1: Epidemiology of AIDS worldwide.

Region	Incidence (millions)	Prevalence (millions)	Deaths (millions)
Globally	33.2	2.5	2.1
Sub-Saharan Africa	25.4	3.1	2.3
East Asia	1.1	0.29	0.051
South and South-East Asia	7.1	0.89	0.49

Table-2: (HIV/AIDS in Pakistan)

Adult HIV Prevalence (%)	People living with HIV/AIDS	People dying with AIDS	ARV Need	People on ARV Treatment
0.1	85,000	3,00	12,000	<200

Table-3: Transmission of AIDS.

Route	High Risk Groups
Sexual	Unprotected sex, homosexuals, multiple sex partners
Blood or blood product route	IV drug abusers, haemophiliacs, recipients of blood products, reuse of
	Needles in third world countries, health care workers, people receiving
	Tattoos and piercing of different parts of their body e.g. ear, tongue, skin etc.
Mother-to-child transmission (MTCT)	During pregnancy and intrapartum route at childbirth. Breast feeding
Saliva, tears and urine of infected individuals	Potential risk of transmission is negligible

Table-4: The pathophysiology of AIDS.

Immune defences	Pathology
Cd4 + Lymphocytes	Place for most of HIV replication. Progressive depletion due to sequestration in inflammed
	Lymphoid tissues, diminished production due to cellular hypo productivity in bone marrow
CDB + T lymphocytes	In early HIV infection, CD8+ T-cell numbers tend to increase, reflecting expansion of
	Memory Cd8+ T cells, particularly HIV-reactive cells. In advanced stages CD 8 decreases.
B lymphocytes and antibody production	Hyper activation and hypo responsiveness
Monocytes, macrophages	Impaired function

Table-5: Indications for starting therapy for AIDS.

Symptomatic or Cd4 < 200	Definitely start treatment
Cd4 200-350	Evidence supporting treatment.
CDR > 350	Data equivocal. Some cohort studies show treatment benefit, but magnitude of difference is small.
Viral load (VL) > 100,000	Independent indicator of need for therapy

Table-6: Indications for prophylaxis against opportunistic infections encountered in AIDS.

CD Count < 200	Pneumocystis jiroveci pneumonia
CD Count < 100	Mycobacterium avium complex and toxoplasmosis
PPD reaction > 5mm Induration	Mycobacterium tuberculosis
CD Count < 50 and CMV antibodies present	Independent indicator of need for therapy

Table7: Treatment of aids-HAART (highly active antiretroviral therapy) .

Group	Mechanism	Sub Group	Dose	Side Effects	Remarks
Nucleoside reverse transcriptase inhibitors (NRTI)	Prevent HIV DNA synthesis	Lamivudine (3TC)	300 mg OD	Peripheral neuropathy, Rhabdomyolysis	Tenofovir–Emtricitabine combination has superior outcome in this group. Other options are Abacavir plus lamivudine, or zidovudine plus lamivudine. Lactic acidosis and hepatic steatosis is common with all NRTI. Long-term exposure is associated with mitochondrial dysfunction.
		Tenofovir	245 mg OD	Renal dysfunction	
		Abacavir	300 mg BD	Hypersensitivity reactions	
		Didanosine (ddI)	400 mg OD	Peripheral neuropathy, Pancreatitis	
		Emtricitabine (FTC)	200 mg OD	Reversible skin pigmentation	
		Zidovudine (ZDV, AZT)	300 mg BD	Anemia, Neutropenia	
		Stavudine (d4T)	40mg BD	Lipoatrophy	
Non-nucleoside reverse transcriptase inhibitors (NNRTI)	Inhibitors of DNA synthesis	Efavirenz	600 mg OD	CNS Toxicity, Teratogenic	Efavirenz is preferred as first line anchor drug.
		Nevirapine	200 mg BD	Stevens-Johnson syndrome, Hepatotoxicity	
Protease inhibitors	These drugs Prevent cleavage of HIV proteins and viral maturation	Atazanavir	200 mg OD	Unconjugated hyperbilirubinemia	Ritonavir plus Lopinavir are currently the preferred option for first line protease inhibitors. There is increased risk of myocardial infarction which seems to be associated with protease inhibitors.
		Darunavir	600 mg BD	Generally well tolerated	
		Indinavir	800 mg TDS	Renal stones	
		Lopinavir	400 mg BD	Gastrointestinal symptoms, Lipid abnormalities	
Entry inhibitors	Prevent entry of HIV into CD4 cells	Enfuvirtide	90 mg S/C BD	Severe local site reactions	Used in patients with highly resistant HIV.
HIV integrase inhibitors	Prevent integration of HIV DNA into the host genome	Raltegravir, Elvitegravir			

In Pakistan the incidence is shown in **Table 2**. [2]

In Pakistan HIV prevalence rates among intravenous drug abusers ranged between 10 to 50 percent in and around Quetta, Faisalabad, Hyderabad, Karachi, and Sargodha. Surveillance data for 2006 point to a local concentrated epidemic among male sex workers and transgenders in Larkana and Karachi in the Sindh province while prevalence elsewhere is still below 5 percent.[3]

Though development of Highly Active Antiretroviral Therapy (HAART) as effective therapy for HIV infection and AIDS has substantially reduced the death rate from this disease, the number of persons living with AIDS has also increased substantially.[4] In some African countries , Cambodia ,South India and Thailand, better surveillance, behaviour change and death among HIV affected people, has helped to slow the epidemic.[4] However in developing countries only 20 % of HIV infected individuals have access to antiretroviral drugs.[5]

There are different modes of transmission for AIDS and it is shown in **Table 3**.[6,7]

The pathophysiology of AIDS is a bit complicated as it involves immune system and its important components especially lymphocytes. It is highlighted in the **Table 4.**

The clinical features of AIDS comprise a long list however the more often encountered signs and symptoms include fever, night sweats, lymphadenopathy, chills, weakness, maculopapular rash and weight loss. Opportunistic infections e.g. recurrent oral candidiasis, pulmonary tuberculosis, Pneumocystis carinii pneumonia and Cytomegalovirus are also common.[8,9]

The diagnosis of AIDS is extremely important as it should be diagnosed on time otherwise complications may be lethal. Lymphopoenia with depression of the CD4 cell subset is a marker for HIV disease. Mild to moderate neutropoenia and a normochromic, normocytic anaemia and thrombocytopoenia are common.[10] Screening is done by Enzyme-Linked Immunosorbent Assay (ELISA) and confirmation by Western Blot or HIV PCR.[11]

Treatment of AIDS has been entirely revolutionized in the recent past and to make it simplified, Table 5 shows various groups of antiretroviral agents, their mechanism of action, dose and major side effects along with few remarks.[12-25]

Having described the treatment of AIDS as an overall review, it is also important to know about the indications of anti-AIDS therapy as not all patients suffering from AIDS syndrome require all the treatment modalities or therapeutic agents as such. There are certain indications for the treatment of this condition to follow. Table 6 shows this as follows.[26,27,28] First line regimen should include two NRTI and a third "anchor" drug that can be either a NNRTI or a protease inhibitor.[29] Starting HAART may present with Immune reconstitution syndrome that results in worsening of a pre-existing condition or new opportunistic infection especially in those with CD 4 count <50.[30] Interrupting therapy is usually associated with rapid loss of CD4 T cells and is not currently recommended.[31,32]

The antiretroviral therapy may lead to many adverse reactions and the case may become more complicated. Moreover, AIDS syndrome has its own complications including many atypical and opportunistic life threatening infections and its management is shown in Table 7.[33] As shown above there are a number of complications due to AIDS, but quite a few of them can be prevented by giving prophylaxis against those infections depending upon the level of CD counts and various antiviral antibodies which is shown in **Table-8**.[33] As shown above there are a number of complications due to

Table-8: Treatment of complications due to AIDS.

Complications	Treatment
Pneumocystis jiroveci pneumonia	Trimethoprimsulfamethoxazole. Adjunctive corticosteroids in case of hypoxemia.
	Severe Cases: IV pentamidine
Toxoplasmosis	Pyrimethamine and sulfadiazine
Cytomegalovirus	IV ganciclovir
Tuberculosis	Anti tuberculous therapy
Oral candidiasis	Fluconazole for 10-14 days
Kaposi sarcoma (KS)	Cutaneous KS: Alitretinoin gel, Advanced KS: PLD (Pegylated liposomal
	Doxorubicin) and radiotherapy
Anemia	Erythropoietin reduces need for blood transfusions
Mycobacterium avium complex	Clarithromycin, ethambutol and Rifabutin
Cryptococcal meningitis	Amphotericin B
AIDS wasting syndrome	Bisphosphonate and testosterone
Nutritional deficiency	No conclusive evidence that micronutrient and macronutrient supplementation
	reduces morbidity and mortality.

Table-9: Prevention of AIDS.

Route	High Risk Groups
Barrier contraceptives	Reduce the probability of HIV transmission per sex act by as much as 95%.
Male circumcision	Medically performed can reduce the acquisition of HIV infection in men by at least 50%.
Nonoxynol-9	There is no evidence that protects against vaginal acquisition of HIV infection by women
	from men. There is evidence that it may do harm by increasing the frequency of genital lesions.
To reduce mother-to	A combination of zidovudine and lamivudine given to mothers in the antenatal,
child transmission of HIV	intrapartum and postpartum periods and to babies for a week after delivery

AIDS, but quite a few of them can be prevented by giving prophylaxis against those infections depending upon the level of CD counts and various antiviral antibodies which is shown in **Table 9**.[33]

HIV In Pakistan [38]

Pakistan is perceived as a 'high risk low prevalence country' concerning the HIV/AIDS virus. According to official government figures, there are 2,622 HIV and 321 AIDS cases in the country.[39] However, according to UNAIDS estimates, HIV/AIDS cases are under-reported in the country and perhaps prevalent among 70,000 to 96,000 people in the country or 0.1 percent of the adult population.

Recent studies,[40] further indicate that there is a rise in HIV/AIDS and STI cases in the 'high risk groups' with concentrated epidemics beginning in marginalized populations like the intravenous drug users and transvestites in Karachi, which, according to a study conducted by Family Health International (FHI), have a high potential of being passed on into the general population due to a closely weaved social network.[41]

The Pakistan National AIDS Control Programme (NACP) is the one organization that coordinates national AIDS strategies. In the present scenario, HIV/AIDS prevention and control in Pakistan has gained attention due to donor driven pressure and allocations of large amounts of funding ($40 million USD) through a comprehensive, five-year enhanced HIV/AIDS program (2003 2008) executed by NACP under the leadership of the Ministry of Health (Government of Pakistan) with financial assistance

as the Department for International Development (DFID) and Canadian International Development Agency (Canadian CIDA).[42] The contract for the Enhanced Program was signed in 2002; however, the funds were released to the provinces only in 2004.
Pakistan still has a window of opportunity to act decisively to prevent the spread of HIV. Although the estimated HIV burden is still low around 0.1 percent of the adult populationthe country is facing a concentrated epidemic among injecting drug users (IDUs) with HIV
prevalence above 5 percent among IDUs in three of the four provinces. Given linkages between IDUs and other high-risk populations including male and female sex workers, Pakistan needs to scale up targeted intervention urgently to prevent rapid increase in HIV among vulnerable groups.

National Response To HIV/Aids

Government: Pakistan's Federal Ministry of Health initiated a National AIDS Prevention and Control Program (NACP) in 1987. In its early stages, the program was focused on diagnosis of cases that came to hospitals, but progressively began to shift toward a community focus. Its objectives are the prevention of HIV transmission, safe blood transfusions, reduction of STI transmission, establishment of surveillance, training of health staff, research and behavioral studies, and development of program management. The NACP has been included as part of the government's general health program, with support from various external donors. As the government has indicated, more needs to be done. For example, focus on reducing the exposure of high-risk groups is urgently required as is increasing the service coverage of key populations (injecting drug users, female sex workers, men who have sex with men, and prison inmates).
Other priority areas that require attention include improving access to quality treatment and care, strengthening the monitoring and evaluation system, continued advocacy with policy makers and other influential groups, and effective coordination with key agencies including police, jail authorities, and the Ministry of Law and of Narcotics Control.
In early 2001, the Government of Pakistan, through a broad consultative process, developed a national HIV/AIDS Strategic Framework that set out the strategies and priorities for effective control of the epidemic. The government has finalized costed action plans for the next phase of the federal and provincial Programs covering the period from 2009-2013. A draft national AIDS policy and HIV and AIDS Law (both recommending the formation of a National AIDS Council) have been prepared by the National AIDS Control Programme and will be presented to the national cabinet and parliament. Approval of the policy and law would be an important step towards the multi-sectoral dimension of the national response.

Issues and challenges: Priority areas.

Vulnerable and High-risk Groups

- Expand knowledge, access, and coverage of vulnerable populationsparticularly in large citiesto a package of high impact services, through combined efforts of the government and NGOs.
- Implement harm-reduction initiatives for IDUs and safe sex practices for sex workers.
- Make effective and affordable STD services available for high-risk groups and the general population.

General Awareness and Behavioral Change

Undertake behavioral change communications with the following behavioral objectives:

(I) Use of condoms with non-regular sexual partners;
(Ii) use of STI treatment services when symptoms are present and knowledge of the link between STIs and HIV;
(iii) use of sterile syringes for all injections;
(iv) reduction in the number of injections received;
(v) voluntary blood donation (particularly among the age group 18 to 30);
(vi) use of blood for transfusion only if it has been screened for HIV; and
(vii) display of tolerant and caring behaviors towards people living with HIV and members of vulnerable populations.

Increase interventions among youth, police, soldiers, and migrant laborers.

Blood and Blood Product Safety

- Ensure mandatory screening of blood and blood products in the public and private sectors for all major blood-borne infections.
- Conduct education campaigns to promote voluntary blood donation.
- Develop Quality Assurance Systems for public and private blood banks to ensure that all blood is properly screened for HIV and Hepatitis B.

Surveillance and Research

- Strengthen and expand the surveillance and monitoring system.

Implement a second-generation HIV surveillance that tracks sero-prevalence and changes in HIV-related behaviors, including the spread of STIs and HIV, sexual attitudes and behaviors, and healthcare-seeking behaviors related to STIs.

Building Management Capacity

- Continue to build management capacity within provincial programs and local NGOs to ensure evidence-based program implementation.
- Identify gaps in existing programs and continue phased expansion of interventions.

World Bank response

The World Bank is the largest financer of HIV/AIDS programs in Pakistan. It assisted the government's HIV/AIDS efforts through funding the second Social Action Program (1998-2003). In addition, the World Bank is working with the government and other development partners (CIDA, DFID, USAID, UN agencies) to support the government's program through the HIV/AIDS Prevention Project. The Bank is providing US$37.1 million, 75 percent of which is a no-interest credit and 25 percent of which is grant money. The project is supporting HIV prevention services to most at-risk groups, mass media campaigns aimed at raising awareness and reducing stigma, promoting safe blood transfusion, and building management and institutional capacity. The implementation of targeted intervention has made encouraging progress with expanding coverage of an injecting drug users program in Punjab; implementation of service delivery packages for male and female sex workers in Sindh, Punjab, and NWFP; jail inmates in Sindh; and truckers nationwide. The data from three rounds of surveillance indicate that HIV prevention services are making a difference as reflected in a reduction in risk behaviors most notably among injecting drug users. At the same time the current coverage of these interventions is limited, covering barely 15-20 percent of the most at-risk groups of injecting drug users and sex workers. The most important issue relates to mobilizing resources and capacity for scaling up services to the high-risk populations. Significant challenges also relate to building capacity of the federal and provincial programs and of the implementing NGOs.

The Bank is committed to supporting the Government's Program over the next phase, focusing particularly on increasing service coverage of most at-risk groups in all major urban centers, improving access and quality of treatment and care, and strengthening the monitoring and evaluation system.

A three-year antiretroviral treatment programme was started in Pakistan in 2006, which included import of drugs from India. The programme will be available to 8000 infected people at public sector hospitals. Cost of generic treatment was $300-500 a patient a year.

Future

The use of combinations of antiretroviral drugs has proven remarkably effective in controlling the progression of HIV disease and prolonging survival, but these benefits can be compromised by the development of drug resistance. [43] Efforts to produce universally available against HIV have so far yielded disappointing results in phase III trials.[44]

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