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Case Report

Lecture, Overview, Consulting Clinical Case of Hiv, Aids and Drug-Resistant Tb Co-Infection

Dorjmaa D[1], Purevsuren[2], Munkhjargal D[1], Buyankhishig B[1]*, Doljinsuren D[1], Unenchime P[1], Oyunbileg B[1] and Anuzaya P[3]

[1]*Consultant of TB Department, National Center for Communicable Disease, Mongolia*
[2]*Department of Tuberculosis, University of Pecs, UK*
[3]*Department of Tuberculosis, Mongolian National University of Medical Sciences, Mongolia*

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***Corresponding author**

Buyankhishig B, Consultant of TB Department, National Center for Communicable Diseases, Ministry of Health and Sport, Campus Nam-Yan-Ju Street, Ulaanbaatar13335, Mongolia, Tel: 976-95950225;
Email: bb_buyankhishig@yahoo.com

Abstract

TB and HIV (Human Immunodeficiency Virus) co-infection is one of the public health issues. TB is one of the main life-threatening infection for HIV-infected people whether the status of enrollment to the anti-retroviral (ARV) treatment, and a cause of death among these people. The risk of getting TB of HIV-not infected people is 5-10%, but of HIV-infected people it increases up to 50%.

Even Mongolia is the low HIV prevalent country, the HIV, AIDS and drug-resistant TB (DR-TB) has increasing trend. By 2017, totally 52 cases of HIV co-infections have been registered of which 6 were DR-TB cases. Out of these cases 50% (3) were aged 45-54 years old, 33% (2) were 25-44 aged people, 17% (1) were 25-34 years old people. But in terms of sex, all were males. Out of registered 6 cases 66% (4) were cases received the first-line TB drugs treatment prior to enrollment in нь DR-TB treatment. According to DR-TB treatment results, 67% (4) were died, 16.5% (1) were cured, and 16.5% (1) were relapse cases. The mortality among HIV-infected cases that getting DR-TB is high, thus the clinical observation made among cases with the specific clinical manifestations, weak treatment results in order to provide information on the treatment follow-up monitoring and diagnosis for clinical doctors.

Case Report

Disease history: U, 46 years old, male, sex minority. The case was hospitalized in Multidrug-resistant TB (MDR-TB) Clinic of National Center for Communicable Disease (NCCD) in February of 2016 due to symptoms of coughing, chest pain, headache, tingling and nerveless changes in the 2 legs, and the pains in abdominal epigastria, back area. The patient had rushes with itches before 1 month of hospitalization. After 14 days had rushes in the mouth.

HIV infection status of patient was diagnosed in May of 2010 and due to CD4 was 118 cells/ml, Viral load 670000 copies/ml at the time of diagnosis, ARV treatment started in 11 June of 2016 using first-line drugs including Zidovudine 300 mg (AZT)+Lamivudine 150 mg (ZTC)+Nevirapine 200 mg (NVP). Even after ARV treatment CD4 cells reached to 276 cells/ml, Viral load 130 copies/ml was at the second months, in 23 January of 2013 number of CD 4 cells decreased to 189 cells/ml, Viral load increased to 440000 copies/ml, since 22 April of 2013 treatment was changed by Tenofovir 300 mg (TDF)+Lamivudine 300 mg (ZTC)+Efavirenz 600 mg (EFV). Due to consistent interruption of treatment the first line drugs treatment was failed and from 28 October 2013 the treatment was done by second-line Tenofovir 300 mg (TDF)+ Lamivudine 300 mg (ZTC)+Lopinavir/Ritonavir 200/50 mg(LPV/RTV). Patients consistently interrupted the ARV treatment, treatment against opportunistic infections (oral cavity fungus), preventive treatment from opportunistic infections (fungus, pneumocystis pneumonia), and refused of treatment (Shown in Table 1 of follow-up examination of HIV, AIDS) [1-4].

History of Previous Treatment

In March of 2015 the Acid Fast Bacillus (AFB) have been diagnosed by sputum smear examination as 10 mycobacterium revealed as smear positive at the National reference TB Laboratory (NTRL) of NCCD and initiated the first-line TB drugs treatment (2HRES/4HR) at the TB cabinet of Bayanzurkh district (BZD). After 2 months of initiation of treatment patient complained on symptoms of coughing, headache, nausea, vomiting, loss of appetite, night sweating, prickle pains at the left side, back and abdominal pains. Therefore patient was hospitalized at the 1st Ward of TB Clinic of NCCD. The resistance to HRES drugs have been identified in patient by Drug Susceptibility Testing (DST) performed at the beginning of treatment. Thus first-line drugs treatment have been shifted to multi-drug resistant TB (MDR-TB) treatment regimen with the Kanamycin (Km)0.75, Pyrazinamide (Z) 1200mg, Levofloxacin (Lfx) 750mg, Protionamide (Pto)

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500mg, Cycloserine (Cs) 500mg. From this time the symptoms of coughing, sputum production, nasal and rectal bleeding has been continuously increased. After stopping of TB treatment and administration of treatment against allergy (anti-histamines) the symptoms were disappeared. The culture examination results at the 1st, 2nd months of treatment follow-up examination were negative in two consecutive months, sputum smear examination results were negative in 1, 2, 3, 4, 5, 6 consecutive months, gaining of 10 kg in body weight, therefore in 22 January of 2016 patient transferred to the TB cabinet for follow up treatment (Shown in Table 2 as "TB treatment follow-up examination"). After discharging from hospital patient

Table 1: HIV/AIDS monitoring examination.

No.	Date	CD4	CD8	CD3	CD4/CD8	BA cps/ml	ARV
1	2010.05.05	118	1097	1325	0.11	670000	I line-AZT+3TC+NVP
2	2010.08.02	276	1658	2063	0.17	130	
3	2010.11.01	225	1245	1647	0.18		
4	2011.02.15	195	775	1065	0.25		
5	2011.05.20	261	1093	1511	0,24		
6	2011.12.20	265	1199	1604	0.22	20	
7	2012.04.04	291	1117	1607	0.26		
8	2012.07.23	236	2000	2498	0.12		
9	2013.01.23	189	1554	1922	0.12	440000	
10	2013.04.15	135	1778	2047	0.08		I line-TDF+3TC+EFV
11	2013.06.21	119	1600	1949	0.07	1600000	
12	2013.10.09	20	727	884	0.03		
13	2013.10.28	12	306	383	0.04	220000	II line- AZT+3TC+LPV/RITr
14	2014.01.15	163	1995	2438	0.08		
15	2014.05.26	15	681	784	0.02		
16	2014.06.23	119	839	1072	0.14		
17	2014.10.22	165	1151	1461	0.14	59	
18	2015.03.05	144	1054	1335	0.14		SS: AFB positive
19	2015.06.10	14	127	156	0.11	210000	
20	2015.10.21	18	711	816	0.03		
21	2016.01.08	6	455	537	0.01		
22	2016.01.19	11	460	478	0.02	230000	

Table 2: Sputum examination.

Months of treatment		Date	Sputum smear microscopy	Culture	Drug susceptibility test	Mass
Drug susceptible tuberculosis	0	2015.03.11	positive^{10}	positive^{++}		
	1	2015.04				
	2	2015.05.19	negative			50 kg
Multi drug resistant tuberculosis	0	2015.06.10	positive	positive	Resistant to HRES	49 кg
	1	2015.07.08	negative	positive		44 кg
	2	2015.08.10	negative	negative		45 кg
	3	2015.09.14	negative	negative		44 кg
	4	2015.10	NA			49 кg
	5	2015.11.16	negative	negative		50 кg
	6	2015.12.15	negative	negative		53 кg
	7	2016.01.15	negative	negative		60 кg
	8	2016.02.17	positive^{+++}	positive^{++}		53 кg
	9	2016.03.24	negative			50 кg
	10	2016.04.9	Died			

have interrupted ARV and MDR-TB treatments. After 25 days the patients' physical condition became severe and re-hospitalized.

According to the epidemiological questionnaire the sexual partner had HIV-infection and had received the drug susceptible TB treatment in 2011 and on June of 2016 confirmed having the MDR-TB. Patient U. doesn't provided the information about contact to clinical doctor, however the information was provided by family members in 2015.

Physical examination by doctor

The physical condition of patients was moderate at the first time of hospitalization. Patient had clear sense, skin mucous were pale, bruising of surrounding area of eyes, the tongue is laid, white rushes in mouth, disappears by scraping. By auscultation, the left lung doesn't have pulmonary wheezing. Abdominal was normal. Liver and spleen were not palpated. After 14 days of hospitalization patient lost speaks, thus communicated using the signals and gestures. Also the symptoms such as dyspnea, bruising, seizures, delusions, nasal and rectal bleeding has increased.

From neural system

Loss of spatial and time orientation, responded to questions by few words unclear. Performs some command of actions. Patient had weak communication with environment. Smack symptoms, Marynovskii-Rodovich syndrome, dementia complex have been observed in patient.

Laboratory examination: According to the Comprehensive metabolic panel and blood testing the leucocytopenia, thrombocytopenia, erythocytopenia have been revealed and hypoalbuminemia, hypocalcaemia, hypokalemia, hypernatremia, hypoproteinemia were detected by biochemical testing (Examination results show in Tables 3 & 4).

Virology testing: HIV load increased up to 230000 cps/ml, CD4 cells quantity was 6-8, CD3=537, CD8=455, CD4/CD8=0, 01.

Diagnostic examinations

Chest X-ray examination (15 May of 2015): Chest X-ray found the cavernous shades at the lateral zones of I-II intercostal area of left lung. The infiltrative shades in the intermediate area of lung roots were revealed. The lung roots were wide and with infiltrative shades. Sinuses were flat, homogenous shades under the VII costal area (along to the lateral lines), right roots are wide, diaphragm is normal; sinuses are free (Figure 1).

Ultrasound examination (18 Feb 2016): Increased echo of the liver and uneven, liver surface is rough without focal lesions. Biliary duct is lean without gallstones. Spleen not increased. Echo of pancreas is even without focal lesions. Corticomedullary Index (CMI) at the 2 kidneys is widened. Shape and size are normal. Abdominal is without free fluid. Left pleura have liquid (slight dense). Right pleura are without fluid.

Table 3: Blood test (by Tuberculosis treatment month).

		Drug susceptible tuberculosis			Multi drug resistant tuberculosis									
Count	**Normal ranges**	**0**	**1 month**	**2 month**	**0**	**1 month**	**2 month**	**3 month**	**4 month**	**5 month**	**6 month**	**7 month**	**8 month**	**9 month**	**10 month**
		2015.03	2015.04	2015.05	2015.06	2015.07	2015.08	2015.09	2015.1	2015.11	2015.12	2016.01	2016.02	2016.03	2016.04
RBC	3.50-5.50			4.31	3.14	2.68	2.92		3.59	3.89		3.88	3.63	2.35	2.39
MCV	75-100			74.7	76.2	85.4	100.4		92.1	92.4		95.6	90.6	88.1	86.6
RDW%	17-Nov			18.1	22.1	30.5	24.4		14.3	18.1		18.1	13.9		14.4
HCT	35-55				24	22.9	29.3		33.1	36		37.1	32.9	20.7	20.7
PLT	100-400			75	30	104	106		83	77		115	92	9	26
MPV	7.0-11.0			11.1		6.7	6.5		8.7	8.7		7.4	10.5	12.1	12.4
PDW	0.1-99.9					10.7	10.5		12.4	12.6		11.1	11.3		18.4
PCT	0.01-9.99			0.08		0.07	0.06		0.07	0.06		0.08	0.1	0.01	0.03
WBC	3.5-10.0			2.35	1.9	2.1	3		4.1	2.5		5.7	4.52	1.98	0.48
HGB	11.5-16.5			10	8.2	8.2	10		12.6	13		13.1	11.6	7.2	7.4
MCH	25.0-35.0			23.2	26.2	30.8	34.3		35.1	33.6		33.9	32	30.6	31
MCHC	31.0-38.0			31.1	34.4	36	34.2		38.1	36.3		35.5	35.3	34.8	35.7
LYM	0.5-5.0			0.93	0.3	0.8	1		1.1	0.7		0.7	1.36	0.45	0.17
GRAN	1.2-8.0				1.5	1.1	1.8		2.8	1.5		4.8			
MID	0.1-1.5				0.1	0.2	0.2		0.2	0.3		0.2			
LYM%	15.0-50.0				18	38.6	33.9		27.4	31.3		12.7			
GRA%	35.0-80.0				79.3	55.4	58.6		68.9	62		84.4			
MID%	2.0-15.0				2.7	6	7.5		3.7	6.8		2.9			
ESR					50	60	39		45	50		28	51		

Table 4: Biochemical examination (by tuberculosis treatment month).

		Drug susceptible tuberculosis			Multi drug resistant tuberculosis										
Test	Reference ranges	0	1 month	2 month	0	1 month	2 month	3 month	4 month	5 month	6 month	7 month	8 month	9 month	10 month
		2015.03	2015.04	2015.05	2015.06	2015.07	2015.08	2015.09	2015.1	2015.11	2015.12	2016.01	2016.02	2016.03	2016.04
Albumin	35-52			26.67	21.49	32.5	33.6	36.95	35.46	36.3	33.32	38.8	28.1		
ALP IFCC	35-129			60.1	57.1		124	114.9	91.7	91.6	64.7	61.2	59.9	83.6	
AMYLASE	28-100			111.6	115.2		169.9	149.4	170.8	155.4		164.2			
ALAT	0-41			85.2	21.9	1.7	6.7	6.2	18.2	11.1	13.5	39.8	28	18.9	
ASAT	0-40			48.6	56.6	10	37.6	30.3	41.3	33.2	28.8	21.8	70.3	48.3	
Bilirubin total	0-17			22.9	33.6	13.3	7.2	6.8	8.7	8.1	8	11.3	12.4	19.1	
Crea	44-106			58	63	67	65	86	69	65	60	79	81	61	
Calcium	2.15-2.55				5.52		1.95	2.26	2.16	2.18		2.15	1.88	1.89	
Chloride direct	101-110			97.2				108.2				103.1			
Glucose	4.11-5.80			5.29	5.07	4.98	5.24	5.19	4.15	5.12	6.05	6.36	5.12	5.3	
Magnesium	0.70-0.95						1.16	0.75							
Potassium direct	3.70-5.50			3.82	3.98	3.98	3.58	3.84	4.24	3.64	4.04	3.36	3.3	3.71	
Sodium direct	146-157			137.4				149.4	149.5		151.1	145.5	133.4		
Total protein	66-87			71.8	62.9	81.7	81.8	81.9	74.4	72.3	80.8	68	57.7	57.4	
Urea/bun	0-8.30			2.57	2.73	3.78	3.38	3.97	4.17	6.5	7.45	7.96			

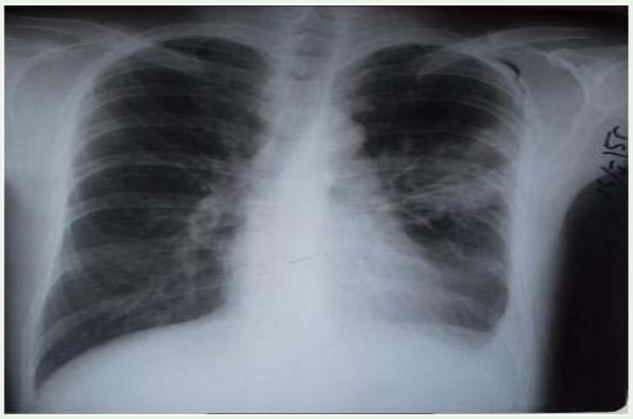

Figure 1: Patient U, 46 years old male, Chest X-ray examination.

Treatment

The treatment by second-line drugs TB treatment (kanamycin, Pyrazinamide, Levofloxacin, Protionamide, and Cycloserine), ARV, treatment to improve blood coagulation, treatment against Disseminated Intravascular Coagulation (DIC), detoxication treatment, protein, anti-fungal treatment were administered. Due to some symptoms of vomiting, the ARV have been stopped and died on 9 April of 2016 due to cardiac and respiratory failures without improvement during the treatment.

Discussion

Due to damages of immune system by HIV the human body becomes unavailable to protect against the diseases. Hereafter Acquired Immunodeficiency Syndrome (AIDS) have been occurred due to the life-threatening conditions such as getting sick of opportunistic infections, cancers, and severe disorders of neurological system. The completely different structures of some domains of glycoproteins of superficial membranes of HIV have been defined by researches, and have 2 types as HIV1 and HIV2. According to study results of researches, HIV1 infection progress is very severe, but the incubation period of infection is relatively short [5] that compare to HIV2 infection.

According to the Handbook of 2010 of World Health Organization (WHO) and Ministerial Order № 397 dated on 20 November of 2009 on "TB care and service guideline", the ARV shall be administered to HIV-infected patient if CD4 cells quantity was less than 350/mm^3 [6,7]. For this case, the CD4 cells quantity at the time of diagnosis was 118cells/mm^3 and ARV treatment have been initiated. However, patient had consistently interrupted ARV treatment and CD4 cells quantity of patients was low (6-18 cell/ml) during the treatment.

In the "TB care and service guideline" approved by Ministerial Order No 397 dated on 20 November of 2009 and Handbook of 2010 of WHO, the close contacts of infectious pulmonary TB patient, and HIV-infected people without TB confirmation are recommended to receive the Isoniazid preventive treatment [8,9]. The patient was not enrolled in the Isoniazid preventive treatment from 2010 of HIV diagnosis to 2015 of TB diagnosis due to the hidden information about contacts.

Moreover, HIV-infected cases recommended to undergo the TB screening every 6 months, and screened for TB using molecular-biologic rapid testing10. This patient consistently involved in the screening for TB and by results examinations done in 2014, and based on the changes of chest X-ray, doctors recommended to undergo

the smear sputum examination for detection of AFB, but patient was not examined. The situations such as patient not pursues the recommendations on the diagnosis and treatment given by doctors, hiding the contact information of TB disease could be main obstacles faced in the early detection of TB.

Gene X-pert (XpertMTB/RIF) shall be used in HIV, AIDS patient to detect TB [10,11]. For our case, even the sputum smear and culture examination have been performed in 2015 at the time of suspected symptoms of TB, the XpertMTB/RIF was not done.

According to the study on "Treatment results of MDR-TB and HIV, AIDS co-infection cases" conducted by doctors from South Africa, the death cases were higher among HIV, AIDS, MDR-TB co-infection cases that received the ARV treatment prior to MDR-TB treatment. The risk of treatment failure and death was higher among cases with risk of low body weight, cavernous changes in the chest X-ray examination, other opportunistic infections, co-morbidities, and anemia [12]. Our case was confirmed as having low body weight, sick of opportunistic infection, and anemia was notified by examination, and even treatment have been continuously administered, there were no improvement in physical condition that makes similarity of with above research.

Some studies observed that the sputum smear examination results could be negative even chest X-ray changes are very high and in majority of cases the Tuberculin test is negative, and symptoms such as weaknesses, fever, loss of body weight symptoms are common, and symptoms such as coughing, sputum with blood are occurred very rare [13]. But for this case except of above mentioned symptoms, the coughing symptoms was very common and even the CD4 cells quantity was low the results of sputum smear examination were positive, and clear clinical manifestations of TB symptoms made the easy diagnosis.

MDR-TB treatment continues for long time, the orally administered first-line TB drugs (Isoniazid, Rifampicin, Ethambutol, and Pyrazinamide) and following TB drugs were recommended depending of drug-resistance. It includes: Groupr A: Levofloxacin, Moxifloxacin, Gatifloxacin; Group B: Amikacin, Kanamycin, Capreomycin, Streptomycin; Group C: Ethionamide, Protionamide, Cycloserine, Linezolid, Clofazamin; Group D: D1- Pyrazinamide, Ethambutol, Isoniazid (high dose), D2- Bedaquiline, Delamanid, D3- Para-amino salicylic acid, Imepenem+Silastatin, Meropenem, Amoxicillin+Clavulanic acid, Thioacetazone.

In intensive phase of treatment 5 drugs shall be administered by 3-4 tablets for 6-8 months, in continuation phase 4 drugs as 304 tablets for each drug shall be administered daily by direct observation [14,15]. Many difficult consequences have been observed such as side effects of many drugs and additional resistance derived from not pursuing the treatment regimen. Many side effects like as rushes in the skin, loss of hearing, psychological changes, complains from digestive organs, changes of thyroid hormones, headache, insomnia observed during the MDR-TB treatment. During the ARV treatment of HIV, AIDS and other preventive treatment of opportunistic infections many drugs are recommended to receive. ARV treatment inhibits the HIV multiplication, and slows the progress of disease to the stage of AIDS [5,7,11]. In our case, the above mentioned complains continued for long time and increased. It was very difficult to diagnose the symptoms related to side effects of drugs and symptoms related to the disease and plan treatment measures.

In case of CD4 cells quantity less of 200 cells/ml, 15% of AIDS patient have AIDS encephalopathy, depression, and behavioral changes progressing in a short time, and forgetfulness, staggered steps, blazing, slowing down the movement of fingers were observed at the early stage of disease, while the dementia, unconscious urination and defecation, seizures, spastic paraparesis, tonic-clonic seizure symptoms at the late stage.

Conclusion

Consistent screening for TB among HIV, AIDS cases recommended to provide, if suspected symptoms of TB have been identified, then the XpertMTB/RIF shall be as a first choice for examination. HIV, AIDS confirmed cases shall be urgently enrolled in the ARV treatment without delay of time, in the preventive treatment against opportunistic infections, administer the drugs in consistent manner. Also provide the health education on ARF treatment benefits, and importance of uninterrupted treatment to patient.

Collection of complete information by contact questionnaire if patient had HIV infection, and enrollment of selected patients to Isoniazid preventive treatment according to inclusion criteria plays crucial role in the decrease of risk of getting TB and death among HIV-infected people.

Acceleration of information, education and communication activities on tuberculosis, HIV, AIDS among general population and provision of psychosocial support to them are required.

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