flora

KLİNİK ÇALIŞMA/RESEARCH ARTICLE

FLORA 2019;24(4):279-287 • doi: 10.5578/flora.68207

Clinical Analysis of Patients with Early HIV Infection in a Low Prevalance Region: Case Series and Review of the Literature

Düşük Prevalanslı Bir Bölgede Erken HIV İnfeksiyonlu Hastaların Klinik Analizi: Olgu Serisi ve Literatür Derlemesi

Fatma ESER[1](İD), Gönül Çiçek ŞENTÜRK[1](İD)

[1] Clinic of Infectious Diseases and Clinical Microbiology, Ankara Diskapi Yildirim Beyazit Training and Research Hospital, Ankara, Turkey

Cite this article as: *Eser F, Şentürk GÇ. Clinical analysis of patients with early HIV infection in a low prevalance region: case series and review of the literature. FLORA 2019;24(4):279-87.*

ABSTRACT

Introduction: *Early HIV infection (EHI) is a highly contagious period in which HIV infection is characterized by non-specific viral infection findings. In this study, we aimed to evaluate patients determined as HIV-positive and followed-up during the EHI period, and to review current data in the literature.*

Materials and Methods: *Patients who had been followed-up with anti-HIV positivity between January 2015 and June 2018 were included into the study. Of these, those who had developed anti-HIV positivity within the last 6 months were considered as EHI. Demographic and clinical data and laboratory findings of the patients with EHI were examined.*

Results: *Eighteen (21.6%) of 83 anti-HIV positive patients were considered as EHI. Sixteen (89%) of the patients were male and mean age was 39.2 (22-65) years. Nine (50%) of the patients had been diagnosed during the differential diagnostic study while 6 (33%) of them had been diagnosed after having been in risky contact. The most common symptoms on admission were fatigue (39%), arthralgia-myalgia (39%), rash (22%), nausea (22%) and anorexia (22%). Ten of the patients (55%) had a history of severe flu infection within the last 6 months. Mean CD4+ cell count was 441.5 (150-1150) 10^3/μL, and mean HIV RNA was 538.975 (3.123-31.249.456) IU/mL on admission. The rate of EHI among newly diagnosed patients was 11.1% (n= 1/9) in 2015, 12.5% (n= 4/32) in 2016, 36.7% (n= 11/30) in 2017, and 16% (n= 2/12) in the first half of 2018. The increase in this rate from 2016 to 2017 was almost statistically significant (p= 0.053). All patients received antiretroviral therapy. No patients died during the follow-up period.*

Conclusion: *This is the first study to evaluate the clinical features of patients with EHI in Turkey. In addition, this study supports that early diagnosis rates have increased in HIV-positive patients in our country.*

Key Words: *HIV; Early HIV infection; Acute HIV infection; Epidemiology; Turkey*

Received/Geliş Tarihi: 28/11/2018 - Accepted/Kabul Ediliş Tarihi: 09/04/2019

ÖZ

Düşük Prevalanslı Bir Bölgede Erken HIV İnfeksiyonlu Hastaların Klinik Analizi: Olgu Serisi ve Literatür Derlemesi

Fatma ESER[1], Gönül Çiçek ŞENTÜRK[1]

[1] Dışkapı Yıldırım Beyazıt Eğitim ve Araştırma Hastanesi, İnfeksiyon Hastalıkları ve Klinik Mikrobiyoloji Kliniği, Ankara, Türkiye

Giriş: *Erken HIV infeksiyonu (EHI), HIV infeksiyonunun, ayırt edici olmayan viral infeksiyon bulguları ile seyreden, bulaştırıcılığın çok yüksek olduğu bir dönemidir. Bu çalışmada EHI ile izlenen hastaların değerlendirilmesi ve beraberinde güncel literatür verilerinin derlenmesi amaçlanmıştır.*

Materyal ve Metod: *Merkezimizde Ocak 2015-Haziran 2018 döneminde yeni tanı anti-HIV pozitifliği nedeniyle takibe alınan hastalar değerlendirildi. Anti-HIV pozitifliği son altı ay içinde gelişmiş olan hastalar EHI olarak değerlendirildi. EHI tanımına uyan hastaların demografik, klinik ve laboratuvar özellikleri irdelendi.*

Bulgular: *Seksen üç hastanın 18 (%21.6)'i EHI olarak değerlendirildi. Hastaların 16 (%89)'sı erkek, ortalama yaş 39.2 (22-65) yıl idi. Hastaların 9 (%50)'unda ayırıcı tanı, 6 (%33)'sında riskli temas öyküsü nedeniyle yapılan tetkiklerde anti-HIV pozitifliği saptandı. Başvurudaki en sık semptomlar sırasıyla halsizlik (%39), kas-eklem ağrısı (%39), döküntü (%22), bulantı (%22), iştahsızlık (%22) idi. Hastaların 10 (%55)'unun öyküsünden son altı ay içinde ağır gribal infeksiyon geçirme öyküsü olduğu öğrenildi. Hastaların başvurudaki ortanca CD4+ sayısı: 441.5 (150-1150) 10^3/μL, ortanca HIV-RNA değeri: 538.975 (3.123-31.249.456) IU/mL olarak bulundu. Yeni tanı ile takibe alınan hastalar arasında EHI oranı 2015 yılında %11.1 (n= 1/9), 2016 yılında %12.5 (n= 4/32), 2017 yılında %36.7 (n= 11/30), 2018 yılı ilk yarısında %16 (n= 2/12) idi. 2016 yılı ile 2017 yılları arasındaki artış oranı anlamlı değere yakın bulundu (p= 0.053). Tüm hastalara antiretroviral tedavi başlandı. Takipleri sırasında kaybedilen hasta olmadı.*

Sonuç: *Bu çalışma, Türkiye'de EHI hastalarının klinik özelliklerini değerlendiren ilk çalışmadır. Ek olarak, bu çalışma ülkemizde HIV pozitif hastaların erken teşhis oranlarının arttığını desteklemektedir.*

Anahtar Kelimeler: *HIV; Erken HIV infeksiyonu; Akut HIV infeksiyonu; Epidemiyoloji; Türkiye*

INTRODUCTION

Despite the reduction in the number of new patients among HIV-infected individuals worldwide, it is increasing every year in Turkey[1,2]. Early recognition of HIV-positivity is very important clinically and epidemiologically[3]. It was reported that the vast majority of patients diagnosed in our country between 1993 and 2006 had been recognized in the late stages of the disease. Ertunç et al. have reported that about half of the patients in Turkey between 1998 and 2013 was diagnosed during the early or asymptomatic period of the disease[4,5].

Acute HIV infection (AHI) is the clinical period manifesting as of viral transmission until detectable levels of serum antigens are produced. Early HIV infection (EHI) covers the AHI period and is characterized with rapid viral replication after transmission, intense immune damage-destruction and immunological response, and the presence of infected cell reservoirs[6,7]. In this period, viral load is very high in the blood (> 10^6 copy/mL) and in the sexual tract, and sexual activity continues as the patient is unaware of the disease[8]. EHI is highly critical clinically and epidemiologically, as the patient is highly contagious during this period[9]. In acute HIV infection, fever, headache, arthralgia-myalgia, loss of appetite, pharyngitis, diarrhea, night sweats, rash, lymphadenopathy, and oral ulcers are common symptoms[10].

There are different definitions in the literature attributing to different durations for staging HIV infection[11,12]. Generally, acute HIV infection is defined as the first month after viral transmission, and EHI defines the first 6 months after transmission[12,13]. Furthermore, recommendations for the treatment and management of EHI are made by considering these definitions[13]. In this study, EHI definition will be used below for both groups of patients.

The aim of this study was to evaluate the demographic and clinical characteristics of the patients followed-up with the diagnosis of EHI in our center and to review the current literature data on this topic.

MATERIALS and METHODS

We retrospectively reviewed the medical files of patients followed-up for newly diagnosed HIV with anti-HIV positivity between January 2015 and June 2018 in our center. Among these patients, only those diagnosed during EHI were included into the study. Only the patients who had been admitted within the last six months and who had a negative laboratory test result for anti-HIV were accepted as EHI. In addition, patients who had no prior history of risky contact and who clearly expressed the risky contact date, and those with symptomatology and laboratory results suggesting EHI were included into the study.

Demographic characteristics, symptoms and findings on admission and laboratory results of the patients were recorded. Antiretroviral therapies administered to the patients, HIV RNA and CD4+ counts and percentages at the beginning of the treatment and during the follow-up were evaluated. Symptoms of fever, sweating, anorexia, weight loss, sore throat, cough, nausea, vomiting, fatigue, abdominal pain, rash, diarrhea, genital lesion, headache, and arthralgia-myalgia were questioned on admission and taken into consideration on the follow-up visits. As laboratory studies, the results of leukocyte, lymphocyte count, hemoglobin, hematocrit, platelet count, blood glucose, urea, creatinine, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), gamma glutamyl transferase (GGT), total bilirubin, direct bilirubin, 25-hydroxy vitamin D, HbA1c, and the urinary albumin/creatinine ratio were recorded. Serological tests of VDRL, HBsAg, anti-HBs and anti-HCV were evaluated.

The assessment of the increase in patient count over the years was made using the Z test with the help of the MedCalc statistical program.

This study was carried out after approval by the local ethics committee of our hospital (Date: 14.05.2018, Decision no. 50/12).

RESULTS

We retrospectively evaluated the medical files of 83 patients followed-up for newly diagnosed HIV with anti-HIV positivity between January 2015 and June 2018 in our center. Among these patients, 18 (21.6%) fulfilled the inclusion criteria and were enrolled in the study.

Sixteen (89%) of the 18 patients were male and the mean age was 39.2 (22-65) years. Four patients declared the homosexual viral transmission route and 12 patients declared the heterosexual route. When we examined the reasons for testing anti-HIV serology test, we noted that in 9 (50%) patients the tests had been requested for differential diagnosis, 6 (33%) for risky contact, and for 3 patients, the tests had been requested during pre-operative preparation procedures.

The number of patients who had a negative anti-HIV test in the last 6 months was 8, and the average time passed over the last negative anti-HIV test of these patients was 3.5 (1-6) months. Eight patients could express the risky contact history clearly, and the average time passed after the risky contact was 3.1 (2-5) months. The anti-HIV serology test results of two patients were compatible with acute HIV infection. Ten patients smoked, 10 patients consumed alcohol, and 1 patient had intravenous drug use in medical history.

Demographic characteristics, viral load and CD4+ cell counts of the patients are presented in Table 1. The symptoms and the laboratory findings of the patients on admission are displayed in Table 2. In the symptom assessment of the patients, we noted that 10 patients (55%) had a history of severe flu infection within the last 6 months and none of the patients had a specific diagnosis at that time. All patients had pathological lymph nodes in one of the cervical, axillary, or inguinal regions. Hepatomegaly was determined in 2 (11%) patients. HBsAg or anti-HCV positivity was not detected in any of the patients. VDRL test positivity was concurrently determined in 3 of the patients.

Two of the patients were diagnosed during the acute HIV infection period and 16 during the

Table 1. Demographic characteristics, viral load and CD4+ cell counts on admission of the patients with early HIV infection

Patient no	Age	Sex	Admission date	Transmission route	Test reason	Interval between high-risk behaviour and diagnosis (month)	Anti-HIV test	Duration between negative anti-HIV test and diagnosis (month)	CD4+ cells (10^3/μL) n (%)	HIV-RNA (IU/mL)
1	51	Male	2015	HS	Risky contact	2	Reactive*		348 (9)	1.642.948
2	39	Male	2016	HS	Differential diagnosis	2	Reactive*		150 (6)	31.249.456
3	30	Male	2016	HS	Differential diagnosis		Reactive*	4	475 (25)	917.206
4	39	Male	2017	HS	Pre-operatif		Reactive*	4	212 (19)	36.503
5	25	Male	2017	HS	Risky contact		Reactive*	3	1150 (25)	400.379
6	46	Male	2016	HS	Differential diagnosis	2	Reactive*		495 (38)	446.338
7	33	Male	2016	HS	Differential diagnosis	5	Reactive*		591 (22)	290.753
8	34	Male	2017	MSM	Risky contact		Reactive*	1	408 (24)	305.737
9	22	Male	2017	MSM	Risky contact		Reactive*	2	912 (38)	3.883.687
10	28	Male	2017	MSM	Differential diagnosis		Negative-İntermine*		587 (33)	631.611
11	30	Male	2017	HS	Risky contact	5	Reactive*		220 (20)	252.945
12	30	Male	2017	MSM	Differential diagnosis		Reactive*	6	513 (27)	14.985
13	43	Male	2017	HS	Differential diagnosis		Reactive*	2	351 (27)	1.327.009
14	39	Male	2017	HS	Pre-operatif	3	Reactive*		312 (24)	112.888
15	35	Male	2017	HS	Risky contact	3	Reactive*		300 (25)	16.958.353
16	58	Female	2017	HS	Pre-operatif		Reactive*	6	555 (37)	3213
17	65	Female	2018	HS	Differential diagnosis	3	Reactive*		224 (18)	14.311.111
18	59	Male	2018	HS	Differential diagnosis		Undeter-mine*,		495 (33)	27.333.333
Mean	39.22222					3.1	p24 Ag-positive**	3.5	461 (25)	5.562.136

* Tested with ELFA
** Tested with ELISA
HS: Heterosexual, MSM: Men sex with men.

Table 2. Symptoms and laboratory findings of the patients with early HIV infection

Symptoms	n (%)	Laboratory findings	Mean (min-max)
Fatigue	7 (39)	Leukocyte (10^3/µL)	5811 (4000-10100)
Arthralgia-myalgia	7 (39)	Lymphocyte (10^3/µL)	1792 (1100-4200)
Rash	4 (22)	Platelet (10^3/µL)	244 (172-435)
Nausea	4 (22)	Hemoglobin (g/dL)	14.5 (11.8-17)
Anorexia	4 (22)	Hematocrit (%)	42.5 (34-51)
Headache	3 (17)	Blood glucose (mg/dL)	97.4 (58-157)
Weight loss	3 (17)	Urea (mg/dL)	28.5 (18-45)
Abdominal pain	3 (17)	Creatinine mg/dL)	0.9 (0.7-1.4)
Sweating	3 (17)	AST (U/L)	36.2 (17-125)
Cough	3 (17)	ALT (U/L)	37 (16-158)
Sore throat	3 (17)	ALP (U/L)	121 (39-332)
Night sweating	3 (17)	GGT (U/L)	89.5 (14-676)
Genital lesion	2 (11)	Total bilirubin (mg/dL)	0.7 (0.4-1.4)
Diarrhea	2 (11)	Direct bilirubin (mg/dL)	0.1 (0.06-0.3)
Fever	2 (11)	25-hydroxy vitamin D (ng/mL)	13.96 (5.5-22.9)
History of severe flu infection with in the last six months	10 (55)	HbA1c (IEX-HPLC) [% (NGSP)[4-6]]	5.4 (2-7.1)
		Urinary albumin/creatinine ratio (µg/mgkre)	8.01 (3.9-19.7)

AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, ALP: Alkaline phosphatase, GGT: Gamma glutamyl transferase.

recent (1-6 months) infection period. One patient had negative-determined (ELFA) laboratory test results and 1 had an undetermined (ELFA) and HIV p24 antigen-positive (ELISA) result while 16 patients had positive results regarding anti-HIV test (HIV ½ discriminating rapid test positive) and confirmatory test (ELFA). At the time of diagnosis, mean CD4+ cell count in 18 patients was 441.5 10^3/µL [min-max= 150-1150 10^3/µL], and mean HIV-RNA value was 538.975 IU/mL [min-max = 3123-31.249.456 IU/mL].

During the study period, a total of 83 patients had been diagnosed with HIV infection, and 21.6% (n= 18) of them were in the EHI period. One of the 9 patients (11.1%) in whom anti-HIV positivity was detected in one year by January 2015, 4 out of the 32 patients (12.5%) were detected in 2016, 11 (36.7%) out of the 30 patients in 2017, and 2 of the 12 patients (16.7%) presenting in the first half of 2018 were accepted as EHI. Year-by-year, the proportion of the patients with EHI among the HIV-positive patients increased, but this difference was not statistically significant (p> 0.05 for each change between two consecutive years), probably due to the small number of the sample size. The increase in the number of patients diagnosed within the EHI period from 2016 to 2017 was not statistically significant, but it was close to the significance level of p= 0.053.

Antiretroviral treatment was initiated in all patients after measurement of the viral load and absolute CD4+ cell count. Seven patients were treated with elvitegravir/cobisistat/emtricitabine/tenofovir alafenamide (EVG/Cobi/FTC/TAF); 7 patients were treated with elvitegravir/cobisistat/ emtricitabine/tenofovir disoproxil fumarate (EVG/Cobi/FTC/TDF), 2 patients with tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) plus dolutegravir (DGT), 1 patient with TDF/FTC plus efavirenz, and 1 patient received the abacavir/dolutegravir/lamivudine (ABC/DTG/3TC) treatment protocol.

No patients died during the follow-up period (3-36 months).

DISCUSSION

The success achieved in life saving targets and goals in patients' access to treatment in HIV pre-

vention programs around the world could not be reached in the measures for prevention of new HIV infections[1]. Year after year, more people are diagnosed with new anti-HIV positivity in our country[2]. It is known that patients have been diagnosed earlier in recent years, but there is no study reporting the rate of EHI among these patients and no report regarding the examination of these cases[4,5,14].

Epidemiology

There are approximately 36.9 (31.1-43.9) million HIV-infected individuals living all over the world, and the number of HIV-infected new individuals is decreasing each year after having peaked in 1996[1]. However, it is estimated that 1.7 million people were newly infected in 2017. Unfortunately, this number is far away from the global 2020 targets for HIV disease[1]. Another serious problem is that 15-25% of HIV-infected patients are unaware of the fact that they are HIV carriers[1,3]. It has been reported that patients diagnosed early in HIV infection comprise mainly young adults, 80-90% are male, and most of them are men sex with men (MSM). Mean age at diagnosis was reported as 27 to 36 years in previous studies involving very large numbers of patients[5,15,16]. In a study by Sargın et al., they have shown that the proportion of MSM among HIV-positive patients in our country is still low[17]. In our study population, mean age of the patients diagnosed with EHI was 39 years and the male sex rate was 89%, which was consistent with the literature[15,16,18]. However, only 1 in 4 of the male patients were MSM. This rate suggests that heterosexual transmission is still an important way in viral spread in Turkey. Similarly, the proportion of IV drug users among HIV-positive patients is still low in our country[18].

Symptoms and Signs

More than half of the HIV-infected patients in the early period suffer from a single symptom[19]. The symptoms of acute HIV infection are usually similar to other viral infections. Symptoms result from the peaking of viremia, immunological response to viral proteins, circulation of the immune complexes of antibodies with acute phase reactants and the production of inflammatory cytokines[6]. The most common signs and symptoms are reported as fever, headache, fatigue and malaise, weakness, cough, and lymphadenopathy. In addition, myalgia, weight loss, night sweats, rash, pharyngitis, gastrointestinal symptoms, and genital ulcers may accompany[10,20,21].

Diagnosis of acute HIV infection at a primary healthcare is difficult due to the fact that its course is similar to other non-specific viral infections; in particular, the clinical findings are similar to influenza[13,21]. In a prospective study involving 155 patients diagnosed with acute HIV infection, only 40% of them were diagnosed as 'acute HIV infection' on first admission although 89% of the patients had reported symptoms[6,15]. Of the 18 patients in our series, 55% had a history of severe flu infectious symptoms during the previous six months and none of the patients had a diagnosis of a specific infection at that time. The most common symptoms at the time of admission were fatigue, arthralgia-myalgia, nausea, anorexia and rash.

Diagnosis and Laboratory Findings

With a thorough anamnesis and physical examination in evaluating early HIV infection, the symptoms and findings associated with EHI can be determined[22]. When the disease is suspected, patients should be questioned in terms of risky sexual behavior, IV drug use, genital ulcer, weight loss, vomiting, diarrhea, arthralgia and fever[3]. In a study, Çerçi et al. have reported that among the patients for whom anti-HIV test was performed, 30.7% of them had undergone the test for the differential diagnosis in those suffering from diarrhea, lymphadenopathy and fever while the test was performed in 21.3% due to risky contact[14]. Similarly, vast majority of the patients in our study were diagnosed with the anti-HIV testing requested for differential diagnosis (50%) or after risky contact (33%).

Laboratory findings during acute HIV infection include leukopenia, lymphopenia, anemia, thrombocytopenia, and elevation of liver enzymes[23]. When the average results of laboratory measurements were examined in our patients, there was no determinant result. We believe that the reason

of this situation was the fact that most of our patients had presented not at the time of acute HIV infection, but during the early HIV infection period. Robb and his colleagues have observed that symptoms and signs most frequently appear just before the viremia peak, and that this time interval corresponds to approximately two weeks after the virus could be detected in blood[20]. In acute infection, mean HIV RNA value was reported to be 726.859 copies/mL (IQR= 167.585-3.565.728 copies/mL) and mean absolute CD 4+ cell count of 408 cells/mm^3 (IQR= 289-563 cells/mm^3). It is also known that although a high viral load is expected during acute infection, the viral load may be below 10.000 copies/mL in a small group of patients[15]. In the study of Volberding and colleagues, 23 patients with acute HIV infection and 50 patients with recent infections (defined as up to 3 months post-transmission) were followed-up. Mean CD4+ cell count was 535 cells/mm^3 (87-1835 cells/mm^3) and the mean plasma HIV RNA level was determined to be 58.000 copies/mL (24.200 to 505.000 copies/mL) for the whole study population[24]. The absolute CD4+ cell count (mean= 441.5) and HIV RNA value (mean= 538.975 IU/mL) of the 18 patients in our study were consistent with those reported in the literature.

In our study group, 3 (16.7%) patients (one female, one MSM) had simultaneous VDRL positivity. HIV and syphilis co-infection rate was found to be 12.9% in the study by Aydin et al., in which 308 HIV patients were enrolled between 2006 and 2013, and they reported that this rate was significantly higher among MSM patients[25]. It has been reported that syphilis has increased in recent years in the United States and that the number of patients rose from 15.9 to 27.4 per 100.000 population from 2012 to 2016[26]. There are also studies reporting that HIV-syphilis co-infection rate is as high as 27% among female sex workers[27].

In our study group, strikingly, 21.6% of the newly diagnosed patients were in the EHI period. Although the difference was not statistically significant due to the low number of patients, the increase in the number of newly diagnosed patients year-by-year emphasizes the importance of EHI. Determination of HIV infection during the EHI period can be made by prospective studies and studies involving viral load screening; therefore, it is difficult to give the proportion of the patients diagnosed during EHI among all HIV-positive patients[15,20]. In studies evaluating HIV-infected patients in our country, the proportion of the patients in the EHI period at the time of diagnosis could not be determined[4,5]. In the study by Çerçi et al., the proportion of patients with AIDS among HIV-positive individuals was reported to be reduced from 61% to 34% ($p< 0.005$) after 2006 compared to the time before[14]. To the best of our knowledge, our study is the first in the literature to provide data regarding EHI from Turkey.

Early diagnosis of HIV-infected persons is very important in many aspects. Early diagnosis of HIV infection means early initiation of antiretroviral therapy. Early initiation of antiretroviral treatment decreases the size of the HIV reservoir and has clear benefits on preventing AIDS and non-AIDS-related morbidity. In addition, the aging of the immune system will be delayed in patients with early treatment. Since a large proportion of this patient group is not aware of HIV/AIDS, they continue to perform high-risk behavior while the frequency of their risky behaviors decreases after diagnosis[28,29]. It is known that contagiousness is 9 to 15 times higher in the EHI period than in the chronic infection period[30]. Suppression of the viral load by antiretroviral therapy provides a significant reduction in the risk of HIV transmission[31-33]. Furthermore, life expectancy also prolongs with the prevention of immunosuppression and opportunistic infections[34,35]. For these reasons, recognition of symptoms and signs of EHI contributes to the reduction of HIV-related morbidity and mortality. It would also make it easier to reach the WHO's 90-90-90 target.

Treatment

Large-scale case studies (4685 patients) have revealed that initiation of treatment, regardless of the CD4+ cell count in asymptomatic patients during the early stages of HIV disease is beneficial[36]. There are two main goals in the initiation of antiretroviral therapy in the early period of the disease. First, to contribute to the

improvement of the health status of the individual and the second, to reduce the risk of viral contagiousness[37].

As in the case of the chronic infection state, initiation of specific treatment is recommended for all patients during the EHI period. The goal of treatment is also to reduce the viral load below the detectable level in this group of patients[13]. The recommended treatment protocol is DTG plus FTC/TDF or FTC/TAF. However, the data on the effectiveness of DTG plus TDF/FTC combination in patients during the EHI period are limited. It is not recommended to start the DTG/ABC/3TC treatment regimen in early HIV patients before the determination of HLA-B*5701 negativity. In the INSIGHT START trial, which proved the necessity and importance of starting treatment in the EHI period, approximately 90% of the patients received the TDF + FTC + efavirenz combination therapy[36]. The outcomes of treatment with single tablet regimens (EVG/Cobi/FTC/TAF, EVG/Cobi/FTC/TDF) in this patient group have not yet been reported with large case series.

In our study group, all patients experienced an increase in CD4+ cell count and a decrease in the viral load after the treatment. It is difficult to comment on the treatment success in our study sample due to the low number of patients, but only one of the 16 patients who reached the 6^{th} month of treatment had a detectable level of blood HIV RNA result.

CONCLUSION

Based on the viral characteristics and symptoms of the disease, these symptoms, although not typical, should be kept in mind in the differential diagnosis to aid in early diagnosis, especially in patients with risk factors. It is clear that awareness of the patients and doctors about this issue is increasing. In this study, we aimed to support the awareness about the early HIV infection period and the current data, having reviewed the data on the disease.

CONFLICT of INTEREST

The authors reported no conflict of interest related to this article.

AUTHORSHIP CONTRIBUTIONS

Concept/Design: FE, GÇŞ

Analysis/Interpretation: FE, GÇŞ

Data Acquisition: FE, GÇŞ

Writting: FE

Critical Revision: GÇŞ

Final Approval: FE, GÇŞ

REFERENCES

1. *Joint United Nations Programme on HIV/AIDS (UNAIDS). Last accesed date: 2018 July. http://wwwunaidsorg/sites/default/files/media_asset/unaids-data-2018_enpdf.*
2. *Tümer A. Last accesed date: 07.11.2017. AIDS nedir? Dünyada ve Türkiye'de HIV/AIDS http://wwwhatamhacettepeedutr/AIDS_web-2017pdf.*
3. *Wood E, Kerr T, Rowell G, Montaner JS, Phillips P, Korthuis PT, et al. Does this adult patient have early HIV infection? The rational clinical examination systematic review. JAMA 2014;312:278-85.*
4. *Ertunc B, Kaya S, Koksal I. Clinico-epidemiological analysis of HIV/AIDS patients. Eur J Med 2016;48:157.*
5. *Celikbas A, Ergonul O, Baykam N, Eren S, Esener H, Eroğlu M, et al. Epidemiologic and clinical characteristics of HIV/AIDS patients in Turkey, where the prevalence is the lowest in the region. J Int Assoc Physicians AIDS Care 2008;7:42-5.*
6. *Cohen MS, Shaw GM, McMichael AJ, Haynes BF. Acute HIV-1 infection. N Engl J Med 2011;364:1943-54.*
7. *Lavreys L, Baeten JM, Chohan V, McClelland RS, Hassan WM, Richardson BA, et al. Higher set point plasma viral load and more-severe acute HIV type 1 (HIV-1) illness predict mortality among high-risk HIV-1–infected African women. Clin Infect Dis 2006;42:1333-9.*
8. *Morrison CS, Demers K, Kwok C, Bulime S, Rinaldi A, Munjoma M, et al. Plasma and cervical viral loads among Ugandan and Zimbabwean women during acute and early HIV-1 infection. AIDS 2010;24:573.*
9. *Fisher M, Pao D, Brown AE, Sudarshi D, Gill ON, Cane P, et al. Determinants of HIV-1 transmission in men who have sex with men: a combined clinical, epidemiological and phylogenetic approach. AIDS 2010;24:1739-47.*
10. *Sanders EJ, Price MA, Karita E, Kamali A, Kilembe W, Bekker L-G, et al. Differences in acute retroviral syndrome by HIV-1 subtype in a multicentre cohort study in Africa. AIDS 2017;31:2541.*
11. *Suthar AB, Granich RM, Kato M, Nsanzimana S, Montaner JS, Williams BG. Programmatic implications of acute and early HIV infection. J Infect Dis 2015;212:1351-60.*
12. *Smith MK, Rutstein SE, Powers KA, Fidler S, Miller WC, Eron Jr JJ, et al. The detection and management of early HIV infection: a clinical and public health emergency. J Acquir Immune Defic Syndr 2013;63:S187.*

13. *Department of Health and Human Services (DHHS). Guidelines for the use of antiretroviral agents in adults and adolescents living with HIV. Last accessed date: 09.07.2017. https://aidsinfonihgov/contentfiles/lvguidelines/glchunk/glchunk_20pdf*

14. *Cerci P, İnkaya A, Alp Ş, Tümer A, Ünal S. Evaluation of 255 HIV/AIDS cases: Hacettepe cohort, Ankara, Turkey. Mikrobiyol Bul 2016;50:94-103.*

15. *McKellar MS, Cope AB, Gay CL, McGee KS, Kuruc JD, Kerkau MG, et al. Acute HIV-1 infection in the Southeastern United States: a cohort study. AIDS Res 2013;29:121-8.*

16. *Braun DL, Kouyos RD, Balmer B, Grube C, Weber R, Günthard HF. Frequency and spectrum of unexpected clinical manifestations of primary HIV-1 infection. Clin Infect Dis 2015;61:1013-21.*

17. *Sargin F, Yildiz D, Aydin OA, Mete B, Gunduz A, Karaosmanoglu HK, et al. Changes in HIV demographic patterns in a low prevalence population: no evidence of a shift towards men who have sex with men. Int J Infect Dis 2016;48:52-6.*

18. *Yemisen M, Altuntas Aydın O, Gunduz A, Ozgunes N, Mete B, Ceylan B, et al. Epidemiological profile of naive HIV-1/AIDS patients in Istanbul: the largest case series from Turkey. Curr HIV Res 2014;12:60-4.*

19. *Richey LE, Halperin J. Acute human immunodeficiency virus infection. Am J Med Sci 2013;345:136-42.*

20. *Robb ML, Eller LA, Kibuuka H, Rono K, Maganga L, Nitayaphan S, et al. Prospective study of acute HIV-1 infection in adults in East Africa and Thailand. N Engl J Med 2016;374:2120-30.*

21. *Henn A, Flateau C, Gallien S. Primary HIV infection: clinical presentation, testing, and treatment. Curr Infect Dis Rep 2017;19:37.*

22. *Yerly S, Hirschel B. Diagnosing acute HIV infection. Exp Rev Anti-infect Ther 2012;10:31-41.*

23. *Başaran NC. HIV enfeksiyonunun doğal seyri. Ünal S, Tümer A (editörler). Güncel Bilgiler Işığında HIV/AIDS. 4. Baskı. Ankara: Bilimsel Tıp Yayınevi, 2017:95-110.*

24. *Volberding P, Demeter L, Bosch RJ, Aga E, Pettinelli C, Hirsch M, et al. Antiretroviral therapy in acute and recent HIV infection: a prospective multicenter stratified trial of intentionally interrupted treatment. AIDS 2009;23:1987.*

25. *Aydin ÖA, Karaosmanoglu HK, Sayan M, Ince ER, Nazlican Ö. Seroprevalence and risk factors of Syphilis among HIV/AIDS patients in Istanbul, Turkey. Cent Eur J Public Health 2015;23:65.*

26. *Centers for Disease Control and Prevention (CDC). 2016 Sexually Transmitted Diseases Surveillance. Last accessed date: July 2018. https://wwwcdcgov/std/stats16/tables/24htm.*

27. *Mutagoma M, Nyirazinyoye L, Sebuhoro D, Riedel DJ, Ntaganira J. Syphilis and HIV prevalence and associated factors to their co-infection, hepatitis B and hepatitis C viruses prevalence among female sex workers in Rwanda. BMC Infect Dis 2017;17:525.*

28. *Marks G, Crepaz N, Janssen RS. Estimating sexual transmission of HIV from persons aware and unaware that they are infected with the virus in the USA. AIDS 2006;20:1447-50.*

29. *Dombrowski JC, Harrington RD, Golden MR. Evidence for the long-term stability of HIV transmission-associated sexual behavior following HIV diagnosis. Sex Transmit Dis 2013;40:41.*

30. *Hollingsworth TD, Pilcher CD, Hecht FM, Deeks SG, Fraser C. High transmissibility during early HIV infection among men who have sex with men-San Francisco, California. J Infect Dis 2014;211:1757-60.*

31. *Cohen MS, Chen YQ, McCauley M, Gamble T, Hosseinipour MC, Kumarasamy N, et al. Prevention of HIV-1 infection with early antiretroviral therapy. N Engl J Med 2011;365:493-505.*

32. *Jia Z, Mao Y, Zhang F, Ruan Y, Ma Y, Li J, et al. Antiretroviral therapy to prevent HIV transmission in serodiscordant couples in China (2003–11): a national observational cohort study. The Lancet 2013;382:1195-203.*

33. *Wood E, Kerr T, Marshall BD, Li K, Zhang R, Hogg RS, et al. Longitudinal community plasma HIV-1 RNA concentrations and incidence of HIV-1 among injecting drug users: prospective cohort study. BMJ 2009;338:b1649.*

34. *Kitahata MM, Gange SJ, Abraham AG, Merriman B, Saag MS, Justice AC, et al. Effect of early versus deferred antiretroviral therapy for HIV on survival. N Engl J Med 2009;360:1815-26.*

35. *Strategies for Management of Antiretroviral Therapy Study Group. CD4+ count–guided interruption of antiretroviral treatment. N Engl J Med 2006;355:2283-96.*

36. *Insight Start Study Group. Initiation of antiretroviral therapy in early asymptomatic HIV infection. N Engl J Med 2015;373:795-807.*

37. *Cohen MS, Dye C, Fraser C, Miller WC, Powers KA, Williams BG. HIV treatment as prevention: debate and commentary-will early infection compromise treatment-as-prevention strategies? PLoS Med 2012;9:e1001232.*

Yazışma Adresi/Address for Correspondence

Uzm. Dr. Fatma ESER

Ankara Dışkapı Yıldırım Beyazıt Eğitim ve Araştırma Hastanesi, İnfeksiyon Hastalıkları ve Klinik Mikrobiyoloji Kliniği,
Ankara-Türkiye

E-posta: fatmacivelekeser@hotmail.com