

Review of Syphilis Patient Records in İzmir State Venereal Diseases Clinic from 1994 to 2004

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Aim: The aim of this study was to evaluate patients attending a sexually transmitted infection (STI) outpatient clinic with a presumptive or definitive diagnosis of syphilis with regard to demographic characteristics, clinical findings, diagnostic criteria, treatment regimens and follow-up data over a 10-year period.

Materials and Methods: The records of patients who had a presumptive/definitive diagnosis of syphilis [according to Centers for Disease Control (CDC) criteria] and who were referred to the İzmir State Venereal Diseases Outpatient Clinic or who were diagnosed in the clinic between 1994 and 2004 were reviewed retrospectively.

Results: A total of 689 patients were included for evaluation; 378 (54.7%) were males and 311 (45.3%) were females. The ages of these patients ranged between 13-77 years, with a mean of 35.2±11.2. One hundred and fifty-three of the cases were sex workers. At the time of admission, 12.3% were considered to be in the primary stage, 17.4% in the secondary stage and 70.3% in the latent stage. The most common clinical findings in symptomatic patients were chancre (12%) and rash (9.2%). Human immunodeficiency virus (HIV) serology was screened in only 19.6% of the patients and two were positive. The most preferred treatment regimen was three doses of 2.4 million units benzathine penicillin (at one-week intervals).

Conclusions: Our results indicate that syphilis is still present in the Turkish population and standard approaches in the treatment and follow-up of patients are lacking.

Key Words: Syphilis, sexually transmitted infections, Turkey

İzmir Deri ve Zührevi Hastalıklar Polikliniğine 1994-2004 Yılları Arasında Başvuran Sifiliz Hastalarına Ait Kayıtların Değerlendirilmesi

Amaç: Bu çalışmada 10 yıllık bir sürede Deri ve Zührevi Hastalıklar Polikliniğine kesin veya olası sifiliz tanısı ile başvuran hastaların demografik özelliklerinin, klinik bulgularının, tanı kriterlerinin, tedavi şekillerinin ve izlem sonuçlarının değerlendirilmesi amaçlanmıştır.

Yöntem ve Gereç: 1994-2004 yılları arasında İzmir Deri ve Zührevi Hastalıklar Polikliniğine başvuran kesin veya olası sifiliz (CDC kriterlerine göre) tanısı ile takip edilen hastalar retrospektif olarak incelenmiştir.

Bulgular: Toplam 689 hasta değerlendirilmiştir, hastaların 378 (% 54.7) erkek ve 311 (% 45.3) kadındır. Yaş ortalaması 13-77 (35.2±11.2) dir. Olguların 153'ü seks işçisidir. Olguların % 12.3'ü primer, % 17.4'ü sekonder, % 70.3'ü latent dönemdedirler. Semptomatik hastalarda en sık karşılaşılan klinik bulgu şankır (% 12) ve döküntü (% 9.2) idi. Human Immunodeficiency Virus (HIV) serolojisi sadece % 19.6 hastada incelenmiş ve iki olguda pozitif bulunmuştur. En sık tercih edilen tedavi şekli üç doz (bir hafta ara ile) 2.4 milyon ünite benzatin penisilin uygulamasıdır.

Sonuç: Çalışmamız sifilizin Türk toplumu için hala güncel olduğunu ve standart tedavi ve takip programlarının eksik olduğuna işaret etmektedir.

Anahtar Sözcükler: Sifiliz, Cinsel Yolla Bulaşan Hastalıklar, Türkiye

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Introduction

Syphilis, with a historical background, has recently appeared as a re-emerging disease entity throughout the world. Notification of syphilis is mandatory in Turkey as in a number of other countries. Determined cases are reported daily to the Directorate of Health by the diagnosing physician.

İzmir is the third most largest city in Turkey with a population of 3,000,000. People migrate to İzmir from every city of Turkey because of its developed employment facilities, industry and business opportunities.

According to the data of the Turkish Ministry of Health in 2004, there were 4154 syphilis patients in our country, 319 of whom live in İzmir (1). The frequency of syphilis is estimated to have increased in recent years parallel to the increase in other sexually transmitted infections (STIs) and human immunodeficiency virus (HIV) infection. While the number of HIV-positive patients diagnosed in 1999 was 86, it was 210 in 2004. Syphilis data is available after 1997. According to these data, the numbers of cases diagnosed in 1997 and 2004 were 3194 and 4154, respectively. However, the official numbers show that the prevalence of the disease is somewhat stable and lower than expected, possibly due to the problems experienced in the reporting and recording system.

There are currently no guidelines for the diagnosis and treatment of STIs on a national basis in Turkey. In addition, genitourinary clinics are not widely available and patients attend many different organizations to seek medical care. Thus, the diagnostic and treatment approaches in syphilis show wide variation and there is still no consensus among the many disciplines managing these cases (2).

The aim of this study was to evaluate patients attending an STI outpatient clinic with a presumptive or definitive diagnosis of syphilis with regard to demographic characteristics, clinical findings, diagnostic criteria, treatment regimens and follow-up data over a 10-year period.

Materials and Methods

İzmir State Venereal Diseases Outpatient Clinic is a governmental organization and is involved in the diagnosis and treatment of STIs excluding the

management of HIV/acquired immunodeficiency syndrome (AIDS) cases. The patient profile of the clinic includes registered sex workers who attend for routine screening or who seek medical care for their complaints, unregistered sex workers who are referred to the clinic by regulatory authorities, and other patients who demand medical care for STIs. We reviewed retrospectively the records of patients who had a presumptive/definitive diagnosis of syphilis according to Centers for Disease Control (CDC) criteria (diagnosis of syphilis was confirmed by examining material from a chancre [infectious sore] using a special dark-field microscope or a blood test) and who were referred to the İzmir State Venereal Diseases Outpatient Clinic or who were diagnosed in the clinic between 1994 and 2004 (3). The study protocol was approved by the İzmir Directorate of Health. Data were extracted from the outpatient clinic records. Patients whose data were inadequate and whose follow-up was irregular were excluded from the study.

The diagnostic approach was to perform Venereal Disease Research Laboratory (VDRL) and *Treponema pallidum* hemagglutination (TPHA) tests concurrently. The routine follow-up schedule of the clinic was to repeat non-specific tests at three or six months following the completion of initial treatment. All serologic investigations were carried out in the İzmir Karşıyaka Public Health Laboratories.

Results

A total of 689 patients were included for evaluation; 378 (54.7%) were males and 311 (45.3%) were females. The ages of these patients ranged between 13 and 77 years, with a mean of 35.2 ± 11.2 . At referral, 41.6% of the cases were married and 58.4% were single. The number of patients working in the sex industry was 153 (21.7%); 132 of them (18.7%) were Turkish female sex workers, 10 (1.4%) were foreign female sex workers and 11 (1.5%) were transsexuals. The remaining patients were distributed among a wide variety of occupational groups. There was no pregnant syphilis case. Sixteen patients were excluded from study due to inadequate data.

Of the patients diagnosed as syphilis, 66.5% had attended the İzmir State Venereal Diseases Outpatient Clinic for the first time and 33.5% had been referred from another center.

At the time of admission, 85 cases (12.3%) were in the primary stage, 120 (17.4%) in the secondary stage and 484 (70.3%) in the latent stage of the disease. There was no case of tertiary syphilis.

The most common clinical findings in symptomatic patients were chancre (12%) and rash (9.2%). VDRL test results were negative in 125 patients. Most (115) of these were cases who had received long-term treatment, who were still under control and had positive TPHA test results. Ten of these 125 were diagnosed as primary syphilis and had chancre. Clinical findings of the patients are shown in Table 1 and their VDRL test results are shown in Table 2. Repeated VDRL tests at three or six months following the completion of initial treatment in primary, secondary and tertiary stages were negative in 51/85, 55/120 and 216/484 patients, respectively. TPHA test results were available for 441 patients. Sixty patients in primary stage, 79 in secondary stage and 317

in latent stage had positive TPHA result with a titer of 1/80 or more. A total of 233 patients did not have TPHA tests.

Sexual partners of 613 patients (88.9%) were not investigated. Of the 76 patients whose sexual partners were evaluated, syphilis serology was positive in 12 (15.8%).

Serologic tests for HIV were performed in 19.6% of syphilis patients and only two patients were positive. Screening of other sexually transmitted diseases was also not performed routinely.

Varying doses of penicillin at varying intervals was the treatment of choice in the majority (77.8%) of patients and antibiotics other than penicillin were used in others (Table 3). The most preferred treatment regimen was three doses of 2.4 million units benzathine penicillin (at one-week intervals).

Table 1. Clinical findings of patients.

Finding	Primary stage (n)	Secondary stage (n)	Total (n)	%
Chancre	85	-	85	12.1
Rash	-	65	65	9.2
Mucous patch	-	35	35	5.1
Condyloma	-	9	9	1.3
Lymphadenopathy	8	12	20	2.8

Table 2. Initial and subsequent Venereal Disease Research Laboratory (VDRL) findings of patients.

Titer	VDRL (initial)			VDRL (repeat)**		
	Primary syphilis	Secondary syphilis	Latent syphilis	Primary syphilis	Secondary syphilis	Latent syphilis*
Negative	10	--	115*	51	55	216
1/4	13	51	99	--	10	29
1/8	17	13	80	2	5	34
1/16	29	27	106	1	5	19
1/32	10	28	64	--	3	10
1/64	6	5	12	--	--	1
Not tested	--	--	4	31	42	175

*Diagnosis of latent syphilis was determined by Treponema pallidum hemagglutination (TPHA).

** Repeated VDRL tests at three or six months following the completion of initial treatment.

Table 3. Antibiotic regimens used to treat syphilis*.

Antibiotic regimen		n	
Tetracycline**		73	
Erythromycin***		47	
Penicillin	Benzathine	3 doses	309
		5 doses	138
		7 doses	107
	Procaine	10 doses	81

*In some patients, two or more regimens were co-administered.

** 4 x 500 mg, 15 days *** 4 x 500 mg, 15 days

Discussion

The first syphilis epidemic in Turkey was reported at the beginning of the 19th century. Since that time a number of epidemics have occurred in many cities, particularly in İstanbul. To fight against the disease, which became widespread after World War I, societies and Venereal Disease Outpatient Clinics were established and laws and regulations were introduced (4). In Turkey, sex workers working in brothels are legally required to undergo vaginal smear examinations and serological inspections related to syphilis, hepatitis B and HIV once every three months (5). Since 1983, syphilis has been included among those diseases for which notification is mandatory.

Syphilis is reported to be more frequent in populations with a lower socioeconomic status, in males and between 15 and 30 years of age (6). The finding of a slightly higher mean age in our study along with the almost 1:1 ratio of men to women suggests that the epidemiologic characteristics of the disease may have changed recently and that the risk for women has significantly increased. While this finding may be attributed to the increasing sexual activity of women due to sociocultural alterations experienced in our country in the last decade, the increasing number of men affected by sexually transmitted diseases who transmit infection to their partners may also play an important role in this variation. The increasing incidence of syphilis among women in Turkey is confirmed by data obtained in other studies (6,7).

Syphilis prevalence in the general population in Turkey is reported to be 0–0.46% (8-11). Syphilis frequency among sex workers and transsexuals in Turkey varies between 8.7% and 31.6% (12,13). A review of the data of the Turkish Ministry of Health regarding the distribution of the number of syphilis cases between 1997 and 2001 gives the impression that it is almost constant with no increasing or decreasing trends, whereas the number of HIV/AIDS cases has significantly increased during the same period (14). This controversial situation suggests that syphilis does not receive the attention it deserves and that the reporting system for syphilis is not efficient.

The clinical findings were in agreement with established knowledge, such as chancre being the most common finding. Since the majority of cases were in the latent syphilis stage, the lack of signs and symptoms in most patients is not surprising (15). The high rate (70.3%) of latent syphilis might have resulted from the incidental finding of seropositivity during blood donation or to the negligence of patients to seek medical care in the symptomatic period. In addition, sex workers and waiters are obligated to have routine controls. Some of these positivities (patients diagnosed as latent syphilis) are determined incidentally during these routine controls. Almost 22% of patients included in the study were individuals providing sex for money. Registered sex workers are responsible for a great proportion of this group since regular follow-up of women working in brothels is mandatory. However, an interesting finding of the study is that the majority of patients referred to the clinic were not sex workers. This may be considered a promising finding since it represents the interest of the community in these clinics and the tendency to seek medical care for STIs.

The VDRL tests were performed in 99.4% of the cases once, in 69% twice and in 52.9% three times or more. VDRL results of third or sixth month controls are shown in Table 2. These findings suggest that the patients were reluctant to attend the follow-up visits. Four patients in whom syphilis tests were not performed had been transferred from other health units with a diagnosis of syphilis and their treatment had already been initiated. A group of 125 patients had negative VDRL results. Of these 125, 115 comprised cases that had received long-term treatment and were still under control. A notable finding of the study was that 10 patients with chancre but negative VDRL test results were

diagnosed as primary syphilis. The VDRL-negative patients with a diagnosis of primary syphilis may be due to early seronegatives (16).

Since VDRL results were not followed up routinely and data were not recorded properly, dynamics of VDRL tests could not be analyzed in all cases. Repeated VDRL tests at three or six months following the completion of initial treatment in primary, secondary and latent stages were negative in 51/85, 55/120 and 216/484 patients, respectively. Patients whose VDRL test was not negative were treated with a longer benzathine penicillin-containing regimen or other regimens (tetracycline or erythromycin).

Coexistence of sexually transmitted diseases is frequent. Therefore, screening of those patients who received a diagnosis of syphilis for other STIs, particularly HIV infection, is strongly recommended (17). HIV serology was tested in only 19.7% of the records reviewed; this lower than expected rate may suggest the inefficiency of STI follow-up in our country. In addition, the fact that the government does not reimburse the costs of HIV screening and of screening for other sexually transmitted diseases may have caused this low rate. There were no follow-up records available for patients with positive HIV serology due to the treatment of these patients in different centers.

Treatment had been initiated in 689 patients who received a diagnosis of syphilis; 446 completed their post-treatment follow-ups whereas 243 were lost to follow-up. The treatment of choice in most patients was penicillin at various doses and at varying intervals. In addition, treatments that do not comply with the standard syphilis treatment protocols were also administered in some patients. This suggests that even physicians working in STI clinics are not fully informed regarding STI treatment and it underlines the importance of establishing a national policy concerning STI diagnosis and treatment and preparing consensus guidelines.

The results of this study suggest that approximately one-third of syphilis patients are lost to follow-up, indicating that the notification and follow-up chain in the country is not properly working. Moreover, health care providers working in the STI clinics are not equipped with the knowledge and expertise required for the management of these infections. Thus, there is an urgent need to establish standard treatment protocols and to reach a consensus regarding the management of syphilis. When the incidence of syphilis in the young population is considered, it is obvious that syphilis is still a very important public health problem. Population-based training in addition to the training of health care providers is essential for the control of these infections.

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