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An Outbreak of Early Syphilis in Patients Registered at the City Institute for Skin and Venereal Diseases in Belgrade from 2010 to 2012: a Case Series of 86 Patients

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Abstract

The purpose of this study was to analyze the characteristics of an outbreak of early syphilis registered at the City Institute for Skin and Venereal Diseases in Belgrade, during the period from 2010 to 2012. The study was designed as a case-note review. In a three-year-long period, a total of 86 patients with early syphilis were registered: 33 cases of primary, 31 of secondary and 22 cases of early latent syphilis. Sixty-five (76.5%) of all patients were men who have sex with men, 15 were heterosexual men and 6 were women. The majority of patients were infected in Belgrade, and in 51/86 cases oral sex was the only risk factor. There were 13 HIV-positive patients, all men who have sex with men. Thus, 20% of men who had sex with men in this study were co-infected with HIV.

In conclusion, this outbreak of early syphilis in Belgrade, in which more than two thirds of all patients were men who have sex with men, of whom 20% were HIV-infected, shows the need for: 1) enhanced prevention efforts targeting this group more important than ever, with education and condom use for oral sex as an important part of patient counseling; 2) coordinated and expeditious surveillance, partner services, screening among population at-risk, as well as early diagnosis and treatment.

Key words

Syphilis; Sexual Behaviour; Homosexuality, Male; HIV; Sexual Partners; Disease Transmission, Infectious

In North America and developed countries of northern Europe, by the 1970s, syphilis had become predominantly a disease of men who have sex with men (MSM) (1). However, during the late 1980s, there were renewed outbreaks of heterosexual and congenital syphilis in North America. The outbreaks were mainly observed in commercial sex workers, in whom it was often associated with selling sex for drugs (especially cocaine), and in other persons of lower socioeconomic status.

The incidence of primary and secondary syphilis among MSM is increasing again in many countries. Although the incidence of infectious syphilis in the UK was only 0.3 cases per 100.000 people in 1998, since then, there have been outbreaks in several cities with a previous low prevalence leading to more than 10-fold increase in national incidence rates by 2005. The outbreaks were associated with high rates of partner change, travel or migration links and an increasing predominance of homosexual transmission with a high proportion of human immunodeficiency virus (HIV) co-infection among incident cases. Furthermore, there was a similar trend in increasing number of men who have sex with men who acquired syphilis engaging in unsafe sex in Western Europe [1].

Generally, syphilis is classified as acquired or congenital. Acquired syphilis is divided into early and late syphilis. Early syphilis is defined as any of the first three stages of syphilis: primary, secondary and early latent syphilis. Guidelines of Centers for Disease

Control and Prevention (CDC) and European Guidelines, define early latent syphilis as that acquired within the previous year. According to Guidelines of the World Health Organization (WHO) it is defined as syphilis acquired less than 2 years before referral [2, 3]. Early syphilis is considered infectious, with an estimated risk of transmission of around 60% per partner [4]. Direct contact with lesions of primary and secondary syphilis possess: the greatest risk of transmission. Early latent syphilis is considered infectious because of the 25% chance of relapse to secondary stage [5].

The purpose of this study was to analyze an outbreak of early syphilis registered at the City Institute for Skin and Venereal Diseases in Belgrade (CISVD), from 2010 to 2012, where more than two thirds of all affected patients were men who have sex with men, 20% of whom were HIV-infected. To the best of our knowledge, it was the first reported outbreak of early syphilis among MSM that has occurred in the capital of Serbia.

Methods

A case-note review of patients with primary, secondary or early latent syphilis was undertaken in the City Institute for Skin and Venereal Diseases (CISVD) in Belgrade. The diagnosis of primary and secondary syphilis were made by clinical features and/or positive dark ground microscopy of scrapings and positive serology tests (Venereal Disease Research Laboratory and *Treponema Pallidum* Haemagglutination Assay). The diagnosis of early latent syphilis was made if any of the following criteria were present in the preceding year: a documented seroconversion; 4-fold rise in non-treponemal (reaginic) serum antibody titre in properly treated patients; a history of unequivocal symptoms of primary or secondary syphilis; a sex partner documented to have primary, secondary or early latent syphilis.

Results

From 2010 to 2012, a total of 86 cases of early syphilis were identified at the CISVD (Figure 1) (Table 1). There were 80 male patients, among whom 65 were men who have sex with men (MSM), and 6 female patients among whom 3 were sex workers. The patients' average age was 31 years (range 17 - 58). There were 33 (38.4%) patients with primary syphilis (PS): 31 male patients including 1 with overlapping clinical stage [6], as well as 2 female patients, both with vulvar primary lesions. Twenty eight patients had penile lesions associated with non-tender regional

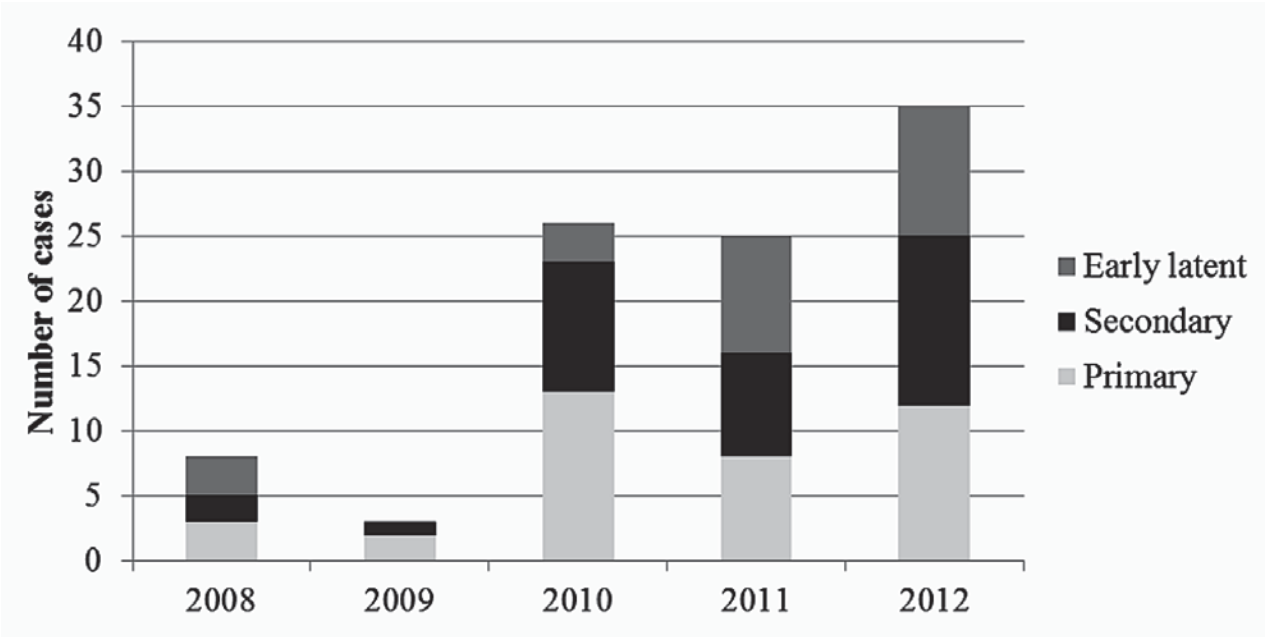

Figure 1. Annual distribution of early syphilis diagnosed at the City Institute for Skin and Venereal Disease, in Belgrade from 2008 to 2012

Table 1. Annual distribution of patients with early syphilis diagnosed at the City Institute for Skin and Venereal Diseases, in Belgrade from 2008 to 2012 classified by the stage of the disease

Year	Patients with primary syphilis (n)	Patients with secondary syphilis (n)	Patients with early latent syphilis (n)	Patients with early syphilis (n)
2008	3	2	3	8
2009	2	1	0	3
2010	13	10	3	26
2011	8	8	9	25
2012	12	13	10	35

n - number of patients

lymphadenopathy while only seven presented with a typical chancre. Anal chancres were found in three cases. Furthermore, atypical presentations of PS were seen in 4/5 of patients as: multiple chancres, painful ulcers resembling genital herpes, nodular lesion and lichen planus-like lesions. All PS cases with penile lesions reported unprotected insertive oral sex with unknown partners one-month before referral to our Institute.

Thirty one patients (36.05%) presented with secondary syphilis (SS). All patients with SS were men who have sex with men: 27 (87.10%) presented with rash, 3 (9.68%) with alopecia syphilitica [7, 8], and 1 (3.22%) with a mucous patch on the tongue as an isolated manifestation of the secondary stage of syphilis [9]. The risk factor for SS was unprotected oral sex alone in 21 cases, and unprotected oral and anal sex in 10 cases.

Primary or secondary syphilis was diagnosed in 64 (74.42%) patients, and among them, there were 3 patients with reinfection. All of them were men who have sex with men in whom reinfection occurred within the past 3 years.

There were twenty two (25.58%) patients with early latent syphilis at the referral: 18 men and 4 women.

Among all 86 patients with early syphilis in this outbreak, there were: 13 HIV-positive, 55 HIV-negative and 16 patients declined testing. All 13 HIV-positive patients were men who have sex with men and 11 (84.61%) were on antiretroviral therapy.

The majority of patients reported to have acquired syphilis in Belgrade. Actually, only 8 patients were infected abroad. Out of all 86 patients, 21 (24.42%) were referred to our Institute due to information provide by their sexual partners.

Almost all patients were treated with a single intramuscular dose of 2.4 million units of benzathine penicillin G, except seven penicillin-allergic patients, who were treated with 14-day course of oral doxycycline (100 mg twice a day).

Discussion

The overall incidence of syphilis in Serbia showed some variations during the last three decades with a peak incidence in 1995 and 2001 [10]. The first increase may be attributed to changes in the country caused by the war, the breakup of former Yugoslavia, economic sanctions and the resulting socioeconomic difficulties as well as the importation of syphilis from the countries of the former Soviet Union [11]. The second peak was in 2001, due to an outbreak of early syphilis in the Institution for Care for Adults with Mental Disorders [12]. Furthermore, since 2010, the incidence showed an increasing trend (Figure 2).

At the beginning of a new millennium, the incidence of syphilis has been increasing worldwide, primarily among MSM. Outbreaks of syphilis in this population have been reported in several European cities [13, 14, 15, 16]. Since 1998, the resurgence of syphilis led to a 25-fold increase in cases of early syphilis among MSM in the United Kingdom [17].

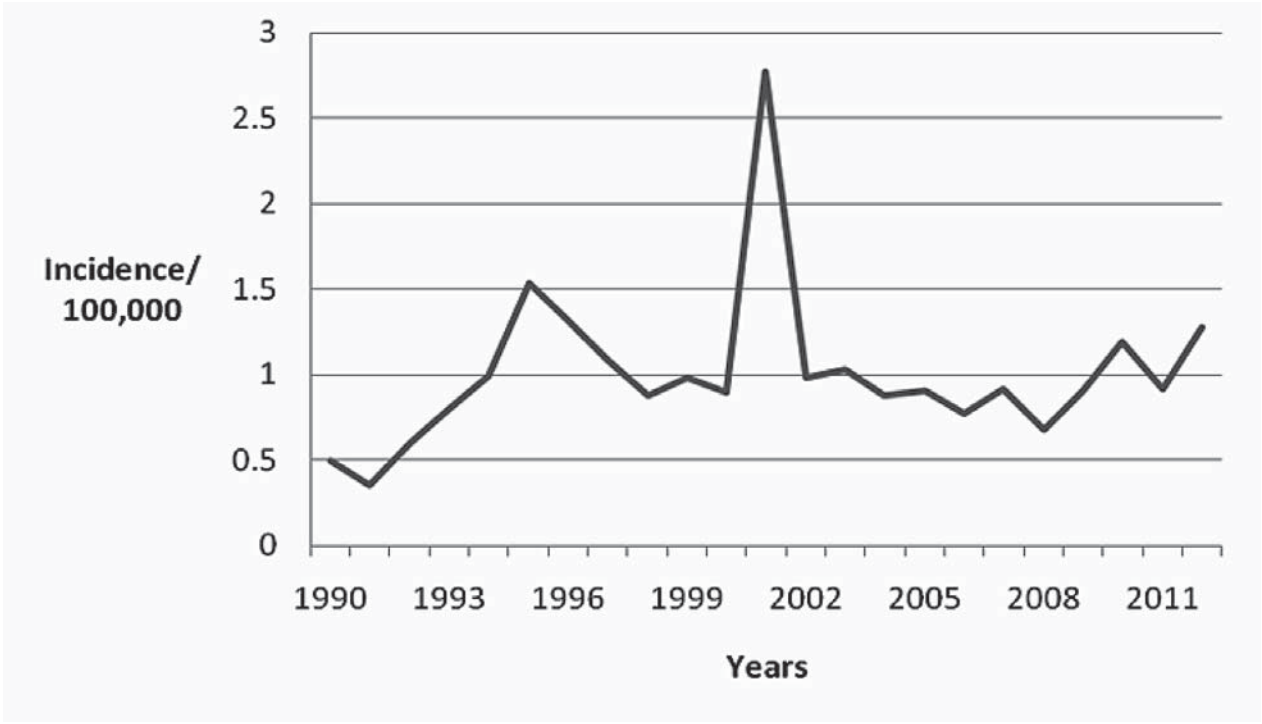

Figure 2. The incidence of syphilis in Serbia from 1990 to 2012

The outbreaks were characterized by rapid increase in homosexual transmission networks, high proportion of HIV coinfection, male to female case ratio of 8:1 and highest rates occurring in men aged 35–44 years and women aged 20–24. Moreover, there was a similar trend in the increasing numbers of men who have sex with men engaging in unsafe sex who acquired syphilis and other bacterial sexually transmitted infections in Western Europe [1]. Thus, during the outbreak of early syphilis in Denmark, 78% of registered cases were MSM, and 37% of them were known to be HIV-positive [18]. According to our results, more than two thirds of all patients (76.5%) with early syphilis in this study were men who have sex with men, and 20% of them were known to be HIV-positive. This is the first reported outbreak of early syphilis among MSM in the capital of Serbia.

Recently described outbreaks of syphilis among MSM revealed that unsafe sex was frequent in this population, with a growing number of casual and anonymous sexual partners and lack of consistent use of condoms. Moreover, increase in syphilis cases may be due to an increased number of psychoactive substance users or because of decreased concern about HIV infection in the era of antiretroviral therapy [19]. The rate of HIV infection is high in patients with syphilis. According to the report of Blocker et al. conducted in 2000, the median HIV-seroprevalence in men and women infected with syphilis in the United States was 15.7 % and seroprevalence among MSM and injecting drug users ranged from 64.3% to 90% and 22.5% to 70.6%, respectively [20]. These data indicate that HIV-infected patients with syphilis may be among the most important transmitters of HIV infection based on their continuous risky behavior as well as well-known biologic effects of genital ulcerations.

The majority of our patients (59.3%) acquired syphilis infection through unprotected oral sex. MSM have low awareness of transmission of other sexually transmitted infections due to diverse types of sexual behavior other than anal intercourse. Oral sex is usually mistaken for "safe" sexual behavior. Moreover, it seems obvious that male patients in this study who had sex with men did not identify oral insertive intercourse as the route for acquiring syphilis, despite the well-known highly contagious oral lesions. These data correlate with other reported outbreaks of syphilis

such as the ones reported in Brighton and Manchester, United Kingdom, where one third of MSM included in the study acquired syphilis through oral sex [21].

Lesions of PS develop after an incubation period of 10 to 90 days (usually 3 weeks). Primary lesions usually last 3 weeks and resolve without treatment. The onset of SS occurs from 2 weeks to 6 months after the resolution of the primary stage (usually 4 weeks). Secondary syphilis lasts 4 weeks, and like primary resolves spontaneously without treatment.

In this study the majority of patients with PS presented with multiple genital ulcers clinically resembling herpes simplex virus infection (22). Similarly, only 31% of males presented with classical manifestations of primary syphilitic chancre in the study of DiCarlo & Martin [23]. These may cause a serious differential diagnostic confusion with other genital ulcers, especially among inexperienced physicians and/or in countries with low incidence of syphilis. The lack of sensitivity of treponemal serologic tests in PS, accentuates the importance of dark ground microscopy, which, if applicable, represents a highly sensitive diagnostic tool in hands of a trained physician, thereby facilitating early diagnosis and intervention [24].

Acquisition of syphilis in this report mainly occurred in Belgrade, the largest city in Serbia, with approximately 2 million citizens. MSM choose to live in large cities which provide more anonymity, less stigma and more meeting places (i.e. sex venues such as parks, bars, public toilets) for sexual contacts [15]. All of the mentioned facilitates spread of sexually transmitted infections.

Contact tracing of sexual partners and treatment of sexual partners affected by sexually transmitted infections, has historically been regarded as an important control measure for syphilis [25]. However, contact tracing is effective only if infected persons are able and willing to cooperate and give information regarding sexual partners. In this report, twenty one persons were identified by their sexual partners. In this outbreak, identification of potentially infected persons by their sexual partners was of a limited contribution to epidemiological data, because majority of partners were casual, anonymous or untraceable. Moreover, patients with diagnosed syphilis were reluctant to identify their partners, despite knowing the importance of their information.

In order to identify other persons at risk of getting syphilis, infected patients were asked to reveal the number of sexual partners they had during the period when they were infectious and to give further information about their partners. The infectious period was estimated on the stage of syphilis: 3 months before the diagnosis for PS, 6 months before the diagnosis for SS, and 1 year before the diagnosis for early latent syphilis.

Conclusion

In summary, the outbreak of early syphilis in Belgrade was mainly transmitted among men who have sex with men. The increasing coinfection with HIV in this population underlines the need for enhanced screening and preventive programs. Risk reduction messages are more important than ever for targeting this group, and condom use for oral sex should be an important part of patient counseling. This outbreak of syphilis also pointed to the need for coordinated and expeditious surveillance, partner services, screening of population at-risk, as well as early diagnosis and treatment.

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Abbreviations

MSM - men who have sex with men
HIV - human immunodeficiency virus
CDC - Centers for Disease Control and Prevention
WHO - World Health Organization
CISVD - City Institute for Skin and Venereal Diseases in Belgrade
PS - primary syphilis
SS - seondary syphilis

Povećan broj pacijenata s ranim sifilisom koji su registrovani u Gradskom zavodu za kožne i polne bolesti u Beogradu u periodu 2010–2012. godine – prikaz serije od 86 slučajeva

Sažetak

Cilj: U ovom radu, osnovni cilj bio je da se analizira povećan broj slučajeva ranog sifilisa koji je registrovan u Gradskom zavodu za kožne i venerične bolesti u Beogradu u periodu 2010–2012. godine.

Materijal i metode: U seriji slučajeva prikazani su podaci prikupljeni od pacijentima sa sifilisom čija je dijagnoza postavljena u Gradskom zavodu za kožne i venerične bolesti u periodu 2010–2012. godine. Sifilis je dijagnostikovan na osnovu kliničke slike i/ili nativnog pregleda u tamnom polju i reaktivnih seroloških testova.

Rezultati: U navedenom trogodišnjem periodu dijagnostikovano je 86 pacijenata sa ranim sifilisom. Trideset tri (38,4%) osobe imale su primarni sifilis, 31 (36%) sekundarni, a kod 22 (25,6%) osobe dijagnostikovan je rani latentni sifilis. Šezdeset pet osoba (76,5%) pripadalo je populaciji muškaraca koji imaju seksualne odnose sa muškarcima a ostalih 15 muškaraca bilo je heteroseksualne orijentacije. Šest

obolelih osoba bilo je ženskog pola. Kod 13 muškaraca koji su imali seksualne odnose sa muškarcima postojala je udružena infekcija HIV-om. Većina obolelih inficirala se u Beogradu, a 51 osoba (59,3%) infekciju je dobila isključivo nezaštićenim oralnim seksom.
Zaključak: Povećan broj registrovanih slučajeva ranog sifilisa u Beogradu, u kojem su više od dve trećine obolelih bili muškarci koji imaju seksualne odnose sa muškarcima od kojih je najmanje 20% bilo inficirano HIV-om, ukazao je na neophodnost promocije bezbednog seksualnog ponašanja, a posebno upotrebe kondoma tokom oralnih seksualnih odnosa. Rana dijagnostika i lečenje sifilisa čine nadasve neophodne preventivne mere u ovoj vulnerabilnoj populaciji.

Ključne reči

Sifilis; Seksualno ponašanje; Homoseksualnost kod muškaraca; Seksualni partneri; Prenošenje infektivnih bolesti

