“He who knows syphilis knows medicine” – the return of an old friend

Michael Rayment, Ann K Sullivan

The roots

But where has all this syphilis come from? Undoubtedly, the outbreak observed in MSM (and possibly the heterosexual outbreak) has been influenced by changes in the HIV pandemic in the era of effective antiretroviral therapy. The decline in self-reported condom use observed in the MSM community (‘safer sex fatigue’), increased rates of partner exchange, and the use of new fora (such as the internet) to meet anonymous sex partners have likely fuelled the epidemic. Indeed, the effectiveness of partner notification, a key method of identifying infection within sexual networks, has been compromised because the majority of syphilis cases (76%) have reported mostly anonymous sexual partners. Control and prevention of syphilis to date has been based on increased access to genito-urinary medicine (GUM) services, partner notification, screening initiatives, outreach to at-risk groups, sexual health promotion and antenatal screening. Despite much investment, there has been no marked reduction in incident cases yet observed, and the delivery of effective intervention remains a challenge to be met.

What does this sudden increase of venereal disease mean to the general physician?

Secondary syphilis, a multi-system disorder seen within six months of acquisition of treponemal infection, may persist or recur over weeks or months, and may present to all types of clinician. The number of cases of ‘other acquired syphilis’ reported by GUM clinics to the HPA annually has
established tertiary syndromes (although either reverse or prevent progression in individuals with latent infection, and may progression towards tertiary syphilis in and thought to have been acquired more than late latent syphilis (asymptomatic infections years). Effective antimicrobial chemotherapy variable incubation periods (typically tens of the three syndromes of tertiary syphilis, in syphilis will progress towards one or more of one-third of all individuals with infectious of the 1950s) suggests that approximately retroactive Oslo Study of Untreated Syphilis. Data from the pre-antibiotic era (such as the clinical types of tertiary syphilis observed. Neurosyphilis refers to any symptomatic infection of the central nervous system (CNS) by Treponema pallidum, and this can occur at any stage of infection – notably during second stage or early latent infection (commonly meningovascular disease – strokes, seizures, and meningitis – or as brainstem and cranial nerve abnormalities, plus ophthalmic and vestibular involvement), or manifest years later with neurological tertiary syndromes affecting the brain and spinal cord parenchyma (such as tabes dorsalis and general paralysis of the insane). Treponemal invasion of the CNS occurs in up to 25% of individuals during early infection, although this will be self-limiting in the majority. An undefined proportion of individuals, however, may present with early neurosyphilis, and it should remain an important differential in young also risen, albeit less dramatically than that observed in infectious syphilis – from 1,076 cases in 1999, to 1,872 cases in 2007 – constituting a 174% increase (English data only). This category comprises cases of late latent syphilis (asymptomatic infections thought to have been acquired more than two years prior to the point of diagnosis) and all cases of tertiary syphilis. This latter subcategory may be subject to underreporting, as many cases of tertiary syphilis are likely to present to non-GUM physicians and be handled beyond the confines of a GUM service. Data are not available on the clinical types of tertiary syphilis observed. Data from the pre-antibiotic era (such as the retrospective Oslo Study of Untreated Syphilis of the 1950s) suggests that approximately one-third of all individuals with infectious syphilis will progress towards one or more of the three syndromes of tertiary syphilis, in approximately equal proportions, and after variable incubation periods (typically tens of years). Effective antimicrobial chemotherapy with penicillin or tetracyclines will prevent progression towards tertiary syphilis in individuals with latent infection, and may either reverse or prevent progression in established tertiary syndromes (although progression may occur despite therapy). Thus, many individuals with latent disease who are given treponemidal antimicrobials for coincident reasons may be inadvertently treated for underlying syphilis. One might argue, therefore, that in the antibiotic era, it is unlikely that the general physician will see resurgence in their out-patient clinics of tertiary syphilis, manifest only years after untreated infection. Perhaps not so... Neurosyphilis refers to any symptomatic infection of the central nervous system (CNS) by Treponema pallidum, and this can occur at any stage of infection – notably during second stage or early latent infection (commonly meningovascular disease – strokes, seizures, and meningitis – or as brainstem and cranial nerve abnormalities, plus ophthalmic and vestibular involvement), or manifest years later with neurological tertiary syndromes affecting the brain and spinal cord parenchyma (such as tabes dorsalis and general paralysis of the insane). Treponemal invasion of the CNS occurs in up to 25% of individuals during early infection, although this will be self-limiting in the majority. An undefined proportion of individuals, however, may present with early neurosyphilis, and it should remain an important differential in young stroke, meningitis, cranial neuropathies, etc., when a sexual risk assessment is undertaken and other clinical features are taken into consideration. There is strong evidence that neurosyphilis at all stages is more common and more symptomatic in HIV-infected individuals, who are disproportionately affected by syphilis infection within the UK, with evidence of increased rates, and persistence of cerebrospinal fluid (CSF) infection after acquisition. Progression towards tertiary neurological syndromes appears hyper-accelerated in this group. Syphilis, itself, appears also to have detrimental effects on the natural history of HIV infection. The optimal management of neurosyphilis in the HIV-infected population remains controversial. **Cardiovascular syphilis** What of cardiovascular syphilis? We would anticipate 10% or more of infected individuals to progress to cardiovascular involvement in the pre-antibiotic era. Cardiovascular syphilis almost certainly still exists in the 21st century. In their recent case series, Roberts et al. demonstrated histological evidence of syphilitic aortitis in 90 adults who died between 1966 and 2000, all of whom had morphological features suggestive of syphilitic aortitis at diagnostic autopsy. All 90 had extensive involvement of the tubular portion of the ascending aorta by the syphilitic process. The aortic arch was also involved in 49 (93%) of 54 patients and the descending thoracic aorta in 47 (90%) of 52 patients. Syphilitic aortitis was the likely cause of death in 23 (26%) of the 90 patients. The authors argue that this series provides evidence of the ongoing existence of cardiovascular syphilis in the antibiotic era. Aman et al. provide an in vivo case – with typical clinical features of dilatation of the ascending aorta, aortic root dilatation and aortic valve regurgitation. This case likely reflects an infection acquired in an area of higher endemicity, but the previous negative antenatal testing history suggests an infection of less than 18 years duration, unaffected by intermittent antibiotic use. One may suspect that the natural history of cardiovascular syphilis may be accelerated in HIV-positive individuals, given the clinical experience of neurosyphilis to date. There is no published evidence to date to support
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this, but we suppose this may be due to the relative immaturity of the syphilis epidemic in this population. In the coming years, might we expect an increase in cases of cardiovascular syphilis mirroring that which we are seeing of early stage disease now?

Guidelines

In GUM services, UK guidelines recommend the routine performance of a chest radiograph in all individuals diagnosed with late latent syphilis, with or without evidence of aortic disease. Any individual with a radiograph suggestive of aortic disease ought to be referred to a cardiologist for evaluation prior to antimicrobial therapy. Steroid therapy is recommended in cardiovascular syphilis to prevent potential consequences of the Jarisch–Herxheimer reaction. Conversely, UK guidelines for the management of aortic regurgitant valves and newly published US guidelines for the management of thoracic aorta disease place little (if any) emphasis on the routine testing for syphilis infection in adults presenting with these conditions. In light of the changing epidemiology of this condition, we would strongly argue that serological screening ought to be undertaken in all patients with dilated ascending aortas, with or without aortic regurgitation, and in those with coronary ostial lesions. Screening is sensitive and widely available, and referral to GUM services should be made in all cases with positive serology, for antimicrobial therapy and contact tracing to be undertaken.

Of course, as I hope we have exemplified, the syphilitic may present to any number of healthcare professionals throughout the course of their illness. To that we say: “Physician, beware the great imitator”. And, rightfully, be wary more so now than at any other time in the past 50 years.

Conflict of interest

None declared.

Editors’ note

See also the case report by Aman et al. on pages 94–6 of this issue.

References


