Detection of Treponema pallidum DNA in the Serum of an Adequately Treated Patient with Latent Syphilis

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Sir,

A significant decline (≥4×) in the serum titres of venereal diseases research laboratory (VDRL) or rapid plasma reagin (RPR) tests occuring in the weeks after treatment of syphilis with antibiotics is believed to be a reliable marker of a good therapeutic response (1). However, there is a lack of experimental data supporting this statement, and serologically defined treatment failure is relatively common (2, 3). At the same time, it is assumed that *Treponema pallidum* is exquisitely sensitive to penicillin and has not developed resistance, although *T. pallidum* is capable of accepting plasmid DNA and has the potential to acquire resistance (4, 5).

In acquired syphilis the concentration of treponemes in the serum is low, and direct detection of *T. pallidum* in whole blood and serum is complicated (6). Nevertheless, *T. pallidum* can be detected using molecular methods. Liu et al. (7) demonstrated that the polA PCR method is extremely robust and sensitive (the detection limit is about 10–25 organisms) and is applicable as a routine clinical diagnostic test for syphilis.

We report here the finding of treponemal DNA in a serum sample of an adequately treated patient with early latent syphilis who had undergone treatment for syphilis 12 weeks previously.

CASE REPORT

A 29-year-old man developed signs of secondary syphilis, which involved a rash and lymphadenopathy. He was IgM-positive (Syphilis Captia IgM, Trinity Biotech, Ireland) and his initial RPR titre was 1:128. He was treated with penicillin G procaine, 1.5 million units twice daily for 14 days and subsequently with penicillin G benzathine intramuscularly, 2.5 million units weekly over 3 consecutive weeks.

After penicillin treatment his RPR titre decreased rapidly. After three months, the titre droped from 1:128 to 1:4. At the same time, the patient was IgM-negative as assessed by enzyme-linked immunosorbent assay (ELISA). Serological findings suggested clinical recovery. Despite the significant decrease in RPR titres, *T. pallidum* DNA was found in his serum by polA PCR (6). *T. pallidum* DNA was detected by this means in his serum for as long as 12 weeks after treatment. A follow-up sample taken 9 months later was PCR-negative.

DISCUSSION

Treponemicidal concentrations of penicillin are ≥0.018 mg/l and are easily achievable in serum by parenteral administration of penicillin. However, some treatment regimens (e.g. benzathine penicillin) do not reliably produce adequate levels of penicillin in the central nervous system. Invasion of the cerebrospinal fluid by *T. pallidum* is common among adults who have primary or secondary syphilis (but it should be noted that neurosyphilis develops in only a limited number of patients). As assessed using a rabbit model (8), there are particularly neuroinvasive *T. pallidum* strains, and the clinical phenotype of infection varies with infecting strain. In some cases, *T. pallidum* could avoid eradication via the central nervous system.

In man, there are findings of treponemal DNA in the cerebrospinal fluid several months after syphilis treatment (9), but little is known about the mechanism of clearance of the treponemal DNA from the cerebrospinal fluid in comparison with the bloodstream.

PCR cannot differentiate between dead and live organisms, which is a shortcoming of PCR, especially in checking the efficacy of treatment. However, Wicher et al. (10) found in rabbit experiments that injected *T. pallidum* chromosomal DNA is eliminated from the bloodstream very quickly; within 48 h.

According to the animal model of syphilis, the clearance of treponemal DNA from the bloodstream is proportional to *T. pallidum* viability and is much more rapid in the case of DNA of dead bacteria in comparison with live ones. A heat-killed Nichols strain of *T. pallidum* is removed from the blood of non-immune rabbits within 14 days, while live strains remain detectable in half of the samples taken from previously non-immune individuals for at least 2 months (11).

Wicher et al. (11) found that PCR correlates almost 100% with the rabbit infectivity testing and suggested that in a treated patient, when taking material for examination 2–3 weeks after treatment, positive PCR indicates treatment failure. However, further research is needed to determine whether these findings can be applied fully to similar clinical situations.

Patients with latent syphilis involved in previous studies that detected treponemal DNA from the bloodstream were untreated or their status was unknown (12, 13). Thus, we believe that the case described here

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is the first report of a *T. pallidum* DNA finding in the serum of an adequately treated patient with documented serological signs of recovery.

Although further evaluation is needed, because the finding was made from one sample, the case reported here may help to reveal the weak points of the present approach to treatment evaluation in latent syphilis, which (especially in routine settings) is almost completely based on serology.

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