A memorable case of secondary syphilis
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A 50-year-old female with no significant medical history suffered an 18-month-long illness with recurrent painful mouth lesions that culminated in mucous patches (Figure 1), together with headaches and episodes of blurred vision, recurrent anogenital lesions, and near-continuous fatigue and arthralgias. She had no skin manifestations beyond a transient palmar rash.

Over a 12-month period she was reviewed by dentistry, general surgery, general medicine, gynaecology, ophthalmology, gastroenterology, rheumatology and dermatology services—over 18 specialist appointments were attended. Investigations for auto-immunity and HIV infection were negative. Biopsies from vulva, perineum and mouth showed nonspecific inflammatory changes. Given a provisional diagnosis of autoimmune disease, she was treated with immune suppression, including Azathioprine, Infliximab, intravenous methylprednisone and multiple courses of oral glucorticoids. No treatment was helpful.

Figure 1: Mucous patches on hard palate.
On later review of the oral biopsy histopathology, a preponderance of plasma cells prompted consideration of syphilis. Serology confirmed infection (RPR 1:128; TPPA reactive), and the patient was seen by Infectious Diseases. Despite reporting most recent sexual activity as four years prior, she had clinical secondary-stage syphilis—atyypical in its duration and unremitting course. The patient claimed the painful oral mucous patches had been unchanged for several months. Earlier ulcerations had been more discrete and transient. Her headaches were symmetrical, intermittent and frequent, though not disabling, and she had no confusion or focal neurological deficit at any stage; nonetheless, lumbar puncture was performed in light of the immune suppression, and confirmed neurosyphilis (CSF VDRL 1:4). Repeat ophthalmology review excluded ocular syphilis, and audiometry was normal. She was treated with two weeks of intravenous benzylpenicillin, followed by intramuscular benzathine penicillin in the third week.

After a dramatic initial improvement, she re-presented two months later with relapsed fatigue, arthralgias and blurred vision, without mucocutaneous pathology. Ophthalmology found new left eye vitritis. RPR was 1:64. She received a further two weeks of intravenous benzylpenicillin, with prednisone in the first 24hr, followed by four weeks of oral amoxicillin, and has made a slow recovery since. Subsequently, RPR titre at six months from first treatment was 1:32.

Syphilis has re-emerged in recent years, with incidence rates rising in many countries, including New Zealand. This case illustrates an unfortunate delay to diagnosis and an unusually protracted and severe secondary-stage illness in the context of significant intercurrent iatrogenic immunosuppression. It is difficult to know whether the clinical relapse after treatment represented treatment failure or a delayed immunological (hypersensitivity) reaction—though the latter is not well-described in syphilis infection. Compared with baseline titre, the RPR at relapse was not significantly different (one dilution); this does not exclude relapse of infection—particularly in a ‘sanctuary site’ such as the eye. Furthermore, her recent heavy immunosuppression makes interpreting serology tests fraught. Tissue histopathology would be potentially informative, but there was no reasonable site to sample at time of relapse. No other tests are contributory in differentiating between relapse of infection and immunopathology from residual treponemal antigen. In clinical practice, it is usually prudent to repeat relatively safe syphilis treatment when in doubt, and consider prescribing glucocorticoids when the inflammatory response is causing significant tissue injury or threatens organ function.

Syphilis should be considered when investigating any mucocutaneous ulcerative disease, regardless of the presence of traditional risk factors for infection. Given the recent epidemiologic trends, screening selected patients for syphilis infection is worth considering prior to planned immunosuppressive treatment.

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