Mixed HSV-1 and HSV-2 infection in a patient attending a GUM clinic

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Infection with herpes simplex virus (HSV) is usually benign (e.g., oral cold sores); however, beyond its well-known embarrassing and painful symptoms, it can occur in critical anatomical sites (e.g., eye or central nervous system). Furthermore, infection acquired during pregnancy can have serious consequences for the neonate, either before or during delivery.[1,2] Unfortunately, along with many other sexually transmitted diseases, HSV infection is on the increase in the UK, with diagnostic rates highest among those aged 20–24 years.[3,4]

In the past, HSV-1 was normally isolated from the upper half of the body innervated by the trigeminal ganglia, while HSV-2 was isolated from the lower half of the body innervated by the sacral ganglia. But, HSV-1 and HSV-2 can infect both the upper and lower halves of the body, and the proportion of genital HSV-1 is now on the increase and is more common than HSV-2. In part, this may be due to the changing sexual behaviour among young people, with increasing orogenital contact.[5] The physical and psychological morbidity of this recurrent viral disease can be substantial, particularly with the increased risk of human immunodeficiency virus (HIV) transmission with concurrent HSV infection.[6,7]

In collaboration with the genitourinary medicine (GUM) clinic at the West Middlesex University Hospital (WMUH), it was agreed that two viral transport swabs be taken during examination of any suspicious lesions and be sent to the immunology/serology department. One would be couriered to the virology department at Northwick Park Hospital for routine HSV culture, while the second would be processed using a direct antigen immunoassay (Oxoid IDEIA Herpes Simplex Virus). This is an amplified enzyme immunoassay (EIA) currently part of the normal regime of tests offered.

The advantage of using the direct antigen test is that GUM staff receive a preliminary result ('negative' or 'presumptive positive') on the swab within 48 h. The disadvantage is that clinic staff still have to wait for the culture result to see if the infection is HSV type 1 or type 2, as immunoassay does not differentiate between them.

Since December 2007, the laboratory has processed 120 swabs that had associated culture results, the overall sensitivity and specificity being 96.3% and 92.1%, respectively. Age range was 17–77 years and the male:female ratio was 1:1.4. Several results showed no correlation, where the immunoassay was positive and culture negative, and vice versa, but this was to be expected bearing in mind the limitations of the assay.[8,9] In the future, it is hoped that both tests will be replaced with a single polymerase chain reaction method.

However, during this period, an interesting case of mixed HSV-1 and HSV-2 infection was found. In 2007, a 77-year-old male presented to the GUM clinic with recurrent genital sores. Two swabs were taken, one for routine viral culture and one for HSV antigen assay. On initial analysis, the EIA gave an equivocal result but on repeat testing gave a positive result. This was reported as 'presumptive positive'. However, culture results from the virus laboratory showed it to be a mixed infection of HSV-1 and HSV-2.

On reviewing the patient's history, he proved to be a known HIV-positive patient who was on regular treatment. His CD4 count was fairly constant (>400 cells/mm^3) and his viral load was <50 copies/mL. He had been to Thailand in 2006 and visited a commercial sex-worker. On his return to the UK he had developed genital sores, which at that time were negative for HSV by culture. In 2007, he had returned to the GUM clinic complaining of recurrent genital sores and small ulcers. This episode was confirmed as the mixed HSV-1 and HSV-2 infection. The patient was treated with valacyclovir for five days, and no symptoms were apparent on clinical review two months later.

Although unusual, mixed infections are not uncommon. In Thailand, there have been reports of an increasing number of genital HSV-1 cases and mixed HSV infections, both in the local population and in foreigners, possibly as a result of changing sexual behaviour in the AIDS era.[10] It was thought that prior infection with HSV-1 or HSV-2 conferred protection against acquisition of the other type, but other studies suggest the opposite.[11–13]

Various hypotheses have been put forward for the mechanisms involved in mixed infections. Some reports show that a patient can acquire HSV-2 infection after HSV-1 infection, and that the HSV-2 reactivates the latent HSV-1. Alternatively, a patient may be infected with HSV-1 and HSV-2 at the same time, with both transmitted subsequently as a mixed infection to a new host.[14–16]

The association between genital HSV-2 infection and an increased risk for acquisition of HIV type 1 has been well documented and is one of the most common co-infections globally, but it remains undiagnosed and untreated.[17,18] The route of entry is likely to be via mucosal or epithelial disruption, which provides the portal of entry for the HIV, and via recruitment of CD4-positive T lymphocytes during HSV-2 reactivation.

Degree of immunosuppression is an important factor in determining the reactivation rate of HSV-2. There have been reports to show a correlation between the mucosal rate of HSV-2 shedding and plasma HIV-1 RNA level, and an inverse correlation with CD4-positive cell counts.[19] However, although HSV-2 is more commonly shed from HIV patients with lower CD4-positive cell counts, it is also shed in patients with a CD4-positive cell count >400 cells/mm^3.

Unfortunately, from the patient's history, it was impossible to determine whether the current lesions were the result of a primary or recurrent infection with either HSV-1 or HSV-2.

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